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(57) Abstract

The invention relates to the identification of members of a gene family from the human respiratory pathogen Chlamydia pneumoniae, encoding surface exposed membrane proteins of a size of approximately 89–101 kDa and of 56–57 kDa, preferably about 89.6–100.3 kDa and about 56.1 kDa. The invention relates to the novel DNA sequences, the deduced amino acid sequences of the corresponding proteins and the use of the DNA sequences and the proteins in diagnosis of infections caused by C. pneumoniae, in pathology, in epidemiology, and as vaccine components.

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NOVEL SURFACE EXPOSED PROTEINS FROM CHLAMYDIA PNEUMONIAE

The present invention relates to the identification of members of a gene family from the human respiratory pathogen Chlamydia pneumoniae, encoding surface exposed membrane

5 proteins of a size of approximately 89-101 kDa and of 56-57 kDa, preferably about 89.6-100.3 kDa and about 56.1 kDa. The invention relates to the novel DNA sequences, the deduced amino acid sequences of the corresponding proteins and the use of the DNA sequences and the proteins in diagnosis of infections caused by C. pneumoniae, in pathology, in epidemiology, and as vaccine components.

GENERAL BACKGROUND

C. pneumoniae is an obligate intracellular bacteria (Christiansen and Birkelund (1992); Grayston et al. (1986)). It has a cell wall structure as Gram negative bacteria with 15 an outer membrane, a periplasmic space, and a cytoplasmic membrane. It is possible to purify the outer membrane from Gram negative bacteria with the detergent sarkosyl. This fraction is named the 'outer membrane complex (OMC)' (Caldwell et al. (1981)). The COMC (Chlamydia outer membrane complex) 20 of C. pneumoniae contains four groups of proteins: A high molecular weight protein 98 kDa as determined by SDS-PAGE, a double band of the cysteine rich outer membrane protein 2 (Omp2) protein of $62/60~\mathrm{kDa}$, the major outer membrane protein (MOMP) of 38 kDa, and the low-molecular weight lipo-protein Omp3 of 12 kDa. The Omp2/Omp3 and MOMP proteins are present in COMC from all Chlamydia species, and these genes have been cloned from both C. trachomatis, C. psittaci and C. pneumoniae. However, the gene encoding 98 kDa protein from C. pneumoniae COMC have not been characterized or cloned. 30

The current state of C. pneumoniae serology and detection

C. pneumoniae is an obligate intra-cellular bacteria belonging to the genus Chlamydia which can be divided into

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four species: C. trachomatis, C. pneumoniae, C. psittaci and C.pecorum. Common for the four species is their obligate intra cellular growth, and that they have a biphasic life cycle, with an extracellular infectious particle (the elementary body, EB), and an intercellular replicating form (the reticulate body, RB). In addition the Chlamydia species are characterized by a common lipopolysaccharide (LPS) epitope that is highly immunogenic in human infection. C. trachomatis is causing the human ocular infection (trachoma) and genital infections. C. psittaci is a variable group of 10 animal pathogens where the avian strains can occasionally infect humans and give rise to a severe pneumonia (ornithosis). The first C. pneumoniae isolate was obtained from an eye infection, but it was classified as a non-typable Chlamydia. Under an epidemic outbreak of pneumonia in Finland 15 it was realized that the patients had a positive reaction in the Chlamydia genus specific test, (the lygranum test), and the patients showed a titre increase to the untyped Chlamydia isolates. Similar isolates were obtained in an outbreak of upper respiratory tract infections in Seattle, and the 20 Chlamydia isolates were classified as a new species, Chlamydia pneumoniae (Grayston et al. (1989)). In addition, C. pneumoniae is suggested to be involved in the development of atherosclerotic lesions and for initiating bronchial asthma (Kuo et al. (1995)). These two conditions are thought 25 to be caused by either chronic infections, by a hypersensitivity reaction, or both.

Diagnosis of Chlamydia pneumoniae infections

Diagnosis of acute respiratory tract infection with C.

pneumoniae is difficult. Cultivation of C. pneumoniae from patient samples is insensitive, even when proper tissue culture cells are selected for the isolation. A C. pneumoniae specific polymerase chain reaction (PCR) has been developed by Campbell et al.(1992).

Even though Chlamydia pneumoniae has in several studies been detected by this PCR it is debated whether this method is suitable for detection under all clinical situations. The reason for this is, that the cells carrying Chlamydia pneumoniae in acute respiratory infections have not been determined, and that a chronic carrier state is expected but it is unknown in which organs and cells they are present. Furthermore, the PCR test is difficult to perform due to the low yield of these bacteria and due to the presence of inhibitory substances in the patient samples. Therefore, it 10 will be of great value to develop sensitive and specific sero-diagnostics for detecting both acute and chronic infections. Sero-diagnosis of Chlamydia infections is currently based on either genus specific tests as the Lygranum test and ELISA, measuring the antibodies to LPS, or 15 the more species specific tests where antibodies to purified EBs are measured by microimmuno fluorescence (Micro-IF) (Wang et al. (1970)). However, the micro-IF method is read by microscopy, and in order to ensure correct readings the 20 result must be compared to the results with C. trachomatis used as antigen due to the cross-reacting antibodies to the common LPS epitope. Thus, there exists in the art an urgent need for development of reliable methods for species specific diagnosis of Chlamydia pneumoniae, as has been expressed in Kuo et al. (1995); "..a rapid reliable laboratory test of 25 infection for the clinical laboratory is a major need in the field". Furthermore, the possible involvement of C. pneumoniae in atherosclerosis and bronchial asthma clearly warrants the development of an effective vaccine.

30 DETAILED DISCLOSURE OF THE INVENTION

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The present invention aims at providing means for efficient diagnosis of infections with *Chlamydia pneumoniae* as well as the development of effective vaccines against infection with this microorganism. The invention thus relates to species specific diagnostic tests for infection in a mammal, such as a human, with *Chlamydia pneumoniae*, said tests being based on

the detection of antibodies against surface exposed membrane proteins of a size of approximately 89-101 kDa and of 56-57 kDa, preferably of about 89.6-100.3 kDa and about 56.1 kDa (the range in size of the deduced amino acid sequences was from 100.3 to 89.6 except for Omp13 with the size of 56.1 kDa), or the detection of nucleic acid fragments encoding such proteins or variants or subsequences thereof. The invention further relates to the amino acid sequences of proteins according to the invention, to variants and subsequences thereof, and to nucleic acid fragments encoding 10 these proteins or variants or subsequences thereof. The present invention further relates to antibodies against proteins according to the invention. The invention also relates to the use of nucleic acid fragments and proteins according to the invention in diagnosis of Chlamydia 15 pneumoniae and vaccines against Chlamydia pneumoniae.

Prior to the disclosure of the present invention only a very limited number of genes from C. pneumoniae had been sequenced. These were primarily the genes encoding known C. trachomatis homologues: MOMP, Omp2, Omp3, Kdo-transferase, 20 the heat shock protein genes GroEl/Es and DnaK, a ribonuclease P homologue and a gene encoding a 76 kDa protein of unknown function. The reason why so few genes have been cloned to date is the very low yield of C. pneumoniae which can be obtained after purification from the host cells. After 25 such purification the DNA must be purified from the EBs, and at this step the C. pneumoniae DNA can easily be contaminated with host cell DNA. In addition to these inherent difficulties, it is exceedingly difficult to cultivate C. pneumoniae and use DNA technology to produce expression 30 libraries with very low amounts (few μg) of DNA. It has been known since 1993 (Melgosa et al., 1993) that a 98 kDa protein is present in OMC from C. pneumoniae. Even though the protein bands of 98 kDa was mentioned to be part of the OMC of C. pneumoniae by Melgosa, the gene sequences and thus the deduced amino acid sequences have not been determined. Only

bands originating from Chlamydia pneumoniae proteins in general separated by SDS-PAGE are describe therein. However, the gene encoding this protein has not been determined before the present invention. Only a very weak or no reaction with patient sera can be observed to the 98 kDa protein (Campbell et al. 1990) and prior to the work of the present inventors it has not been recognized that the 89-101 kDa proteins are surface exposed or that they in fact is immunogenic. In this report it is described that a number of human serum samples reacts with a C. pneumoniae protein that in SDS-PAGE migrate as 98 kDa. The protein was not further characterized and it is therefore not in conflict with the present application.

Halme et al. (1997) described the presence of human T-cell
epitopes in *C. pneumoniae* proteins of 92-98 kDa. The proteins
were eluted from SDS-PAGE of total chlamydia proteins but the
identity of the proteins were not determined.

Use of antibodies to screen expression libraries is a well known method to clone fragments of genes encoding antigenic parts of proteins. However, since patient sera do not show a significant reaction with the 98 kDa protein it has not been possible to use patient serum to clone the proteins.

It was known that monoclonal antibodies generated by the inventors reacted with conformational epitopes on the surface 25 of C. pneumoniae and that they also reacted with C. pneumoniae OMC by immuno-electron microscopy (Christiansen et al. 1994). Furthermore, the 98 kDa protein is the only unknown protein from the C. pneumoniae OMC (Melgosa et al. 1993). The present inventors chose to take an unconventional 30 step in order to clone the gene encoding the hitherto unknown 98 kDa protein: C. pneumoniae OMC was purified and the highly immunogenic conformational epitopes were destroyed by SDStreatment of the antigen before immunization. Thereby an antibody (PAB 150) to less immunogenic linear epitopes was 35 obtained. This provided the possibility to obtain an

antiserum which could detect the protein, and it was shown that a gene family encoding the 89-101 kDa and 56 proteins according to the invention could be detected in colony blotting of recombinant *E. coli*.

Mice infected with *C. pneumoniae* generate antibodies to the proteins identified by the inventors and named Omp4-15, but do not recognize the SDS treated heat denatured antigens normally used for SDS-PAGE and immunoblotting. However, a strong reaction was seen if the antigen was not heat denatured. It is therefore highly likely that if a similar reaction is seen in connection with human infections the antigens of the present invention will be of invaluable use in sero-diagnostic tests and may very likely be used as a vaccine for the prevention of infections.

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By generating antibodies against COMC from C. pneumoniae a polyclonal antibody (PAB 150) was obtained which reacted with all the proteins. This antibody was used to identify the genes encoding the 89.6-101.3 kDa and 56.1 kDa proteins in an expression library of C. pneumoniae DNA. A problem in 20 connection with the present invention was that a family comprising a number of similar genes were found in C. pneumoniae. Therefore, a large number of different clones were required to identify clusters of fragments. Only because the rabbit antibody generated by the use of SDS-denatured 25 antigens contained antibodies to a high number of different epitopes positioned on different members of the protein family did the inventors succeed in cloning and sequencing four of the genes. One gene was fully sequenced, a second was sequenced except for the distal part and shorter fragments of 30 two additional genes were obtained by this procedure. To obtain the DNA sequence of the additional genes and to search for more members of the gene family long range PCR with primers derived from the sequenced genes, and primers from the genes already published in the database were used. This 35 approach gave rise to the detection of additional eight genes belonging to this family. The genes were situated in two gene

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clusters: Omp12,11,10,5,4,13 and 14 in one cluster and Omp6,7,8,9 and 15 in the second. Full sequence was obtained from Omp4,5,6,7,8,9,10,11 and 13, and partial sequence of Omp12,14. Omp13 was a truncated gene of 1545 nucleotides. The rest of the full length genes were from 2526 (Omp7) to 2838 (Omp15) nucleotides. The deduced amino acid sequences revealed putative polypeptides of 89.6 to 100.3 kDa, except for Omp13 of 56.1 kDa. Alignment of the deduced amino acid sequences showed a maximum identity of 49% (Omp5/Omp9) when all the sequences were compared. Except for Omp13, the lowest homology was to Omp7 with no more than 34% identity to any of the other amino acid sequences. The scores for Omp13 was from 29-32% to all the other sequences.

In the present context SEQ ID Nos. 1 and 2 correspond to

Omp4, SEQ ID Nos 3 and 4 correspond to Omp5, SEQ ID Nos 5 and

correspond to Omp6, SEQ ID Nos 7 and 8 correspond to Omp7,

SEQ ID Nos 9 and 10 correspond to Omp8, SEQ ID Nos 11 and 12

correspond to Omp9, SEQ ID Nos 13 and 14 corresponds to

Omp10, SEQ ID Nos 15 and 16 corresponds to Omp11, SEQ ID Nos

17 and 18 corresponds to Omp12, SEQ ID Nos 19 and 20

corresponds to Omp13, SEQ ID Nos 21 and 22 corresponds to

Omp14, and SEQ ID Nos 23 and 24 corresponds to Omp15.

The estimated size of the Omp proteins of the of the present invention are listed in the following. Omp 4 has a size of 98.9 kDa, Omp5 has an estimated size of 97.2 kDa, Omp6 has an estimated size of 100.3 kDa, Omp7 has an estimated size of 89.7 kDa, Omp8 has an estimated size of 90.0 kDa, Omp9 has an estimated size of 96.7 kDa, Omp10 has an estimated size of 98.4 kDa, Omp11 has an estimated size of 97.6 kDa, Omp13 has an estimated size of 56.1 kDa, Omp 12 and 14 being partial.

Furthermore, SEQ ID No 25 is a subsequence of SEQ ID No 3, SEQ ID No 26 is a subsequence of SEQ ID No 4, SEQ ID No 27 is a subsequence of SEQ ID No 5, SEQ ID No 28 is a subsequence of SEQ ID No 6, SEQ ID No 29 is a subsequence of SEQ ID No 7, and SEQ ID No 30 is a subsequence of SEQ ID No 8.

Part of the omp proteins were expressed as fusion proteins, and mice polyclonal monospecific antibodies against the proteins were produced. The antibodies reacted with the surface of C. pneumoniae in both immunofluorescence and immunoelectron microscopy. This shows for the first time that the 89-101 kDa and 56-57 kDa protein family in C. pneumoniae comprises surface exposed outer membrane proteins. This important finding leads to the realization that members of the 89-101 kDa and 56-57 kDa C. pneumoniae protein family are good candidates for the development of a sero diagnostic test 10 for C. pneumoniae, as well as the development of a vaccine against infections with C. pneumoniae based on using these proteins. Furthermore, the proteins may be used as epidemiological markers, and polyclonal monospecific sera against the proteins can be used to detect C. pneumoniae in 15 human tissue or detect C. pneumoniae isolates in tissue culture. Also, the genes encoding the 89-101 kDa and 56-57 kDa such as the 89.6-100.3 kDa and 56.1 protein family may be used for the development of a species specific diagnostic test based on nucleic acid detection/amplification. 20

The full length Omp4 was cloned into an expression vector system that allowed expression of the Omp4 polypeptide. This polypeptide was used as antigen for immunization of a rabbit. Since the protein was purified under denaturing condition the antibody did not react with the native surface of C. pneumoniae, but it reacted with a 98 kDa protein in immunoblotting where purified C. pneumoniae EB was used as antigen. Furthermore, the antibody reacted in paraffin embedded sections of lung tissue from experimentally infected mice.

A broad aspect of the present invention relates to a species specific diagnostic test for infection of a mammal, such as a human, with *Chlamydia pneumoniae*, said test comprising detecting in a patient or preferable in a patient sample the presence of antibodies against proteins from the outer membrane of *Chlamydia pneumoniae*, said proteins being of a

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molecular weight of 89-101 kDa or 56-57 kDa, or detecting the presence of nucleic acid fragments encoding said outer membrane proteins or fragments thereof.

In the context of the present application, the term "patient 5 sample" should be taken to mean an amount of serum from a patient, such as a human patient, or an amount of plasma from said patient, or an amount of mucosa from said patient, or an amount of tissue from said patient, or an amount of expectorate, forced sputum or a bronchial aspirate, an amount 10 of urine from said patient, or an amount of cerebrospinal fluid from said patient, or an amount of atherosclerotic lesion from said patient, or an amount of mucosal swaps from said patient, or an amount of cells from a tissue culture originating from said patient, or an amount of material which 15 in any way originates from said patient. The in vivo test in a human according to the present invention includes a skin test known in the art such as an intradermal test, e.g similar to a Mantaux test. In certain patients being very sensitive to the test, such as is often the case with 20 children, he test could be non-invasive, such as a superficial test on the skin, e.g. by use of a plaster

In the present context, the term 89-101 kDa protein means proteins normally present in the outer membrane of *Chlamydia pneumoniae*, which in SDS-PAGE can be observed as one or more bands with an apparent molecular weight substantially in the range of 89-101 kDa. From the deduced amino acid sequences the molecular size varies from 89.6 to 100.3 kDa.

Within the scope of the present invention are species

specific sero-diagnostic tests based on the usage of the genes belonging to the gene family disclosed in the present application.

Preferred embodiments of the present invention relate to species specific diagnostic tests according to the invention, wherein the outer membrane proteins have sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24.

When used in connection with proteins according to the present invention the term "variant" should be understood as a sequence of amino acids which shows a sequence similarity of less than 100% to one of the proteins of the invention. A variant sequence can be of the same size or it can be of a different size as the sequence it is compared to. A variant will typically show a sequence similarity of preferably at least 50%, preferably at least 60%, more preferably at least 70%, such as at least 80%, e.g. at least 90%, 95% or 98%.

The term "sequence similarity" in connection with sequences

of proteins of the invention means the percentage of
identical and conservatively changed amino acid residues
(with respect to both position and type) in the proteins of
the invention and an aligned protein of equal of different
length. The term "sequence identity" in connection with

sequences of proteins of the invention means the percentage
of identical amino acid with respect to both position and
type in the proteins of the invention and an aligned protein
of equal of different length.

Within the scope of the present invention are subsequences of one of the proteins of the invention, meaning a consecutive stretch of amino acid residues taken from SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24. A subsequence will typically comprise at least 100 amino acids, preferably at least 80 amino acids, more preferably at least 70 amino acids, such as 50 amino acids. It might even be as small as 10-50 amino acids, such as 20-40 amino acids, e.g. about 30 amino acids. A subsequence will typically show a sequence homology of at least 50%, preferably at least 60%, more

preferably at least 70%, such as at least 80%, e.g. at least 90%, 95% or 98%.

Diagnostic tests according to the invention include immunoassays selected from the group consisting of a direct or indirect EIA such as an ELISA, an immunoblot technique such as a Western blot, a radio immuno assay, and any other non-enzyme linked antibody binding assay or procedure such as a fluorescence, agglutination or precipitation reaction, and nephelometry.

- A preferred embodiment of the present invention relates to species specific diagnostic tests according to the invention, said test comprising an ELISA, wherein antibodies against the proteins of the invention or fragments thereof are detected in samples.
- A preferred embodiment of the invention, is an ELISA based on detection in samples of antibodies against proteins of the invention. The ELISA may use proteins of the invention, or variants thereof, i.e. the antigen, as coating agent. An ELISA will typically be developed according to standard methods well known in the art, such as methods described in "Antibodies; a laboratory manual", Ed. David Lane Harlow, Cold Spring Habor laboratories (1988), which is hereby incorporated by reference.

Recombinant proteins will be produced using DNA sequences
obtained essentially using methods described in the examples below. Such DNA sequences, comprising the entire coding region of each gene in the gene family of the invention, will be cloned into an expression vector from which the deduced protein sequence can be purified. The purified proteins will be analyzed for reactivity in ELISA using both monoclonal and polyclonal antibodies as well as sera from experimentally infected mice and human patient sera.

From the experimentally infected mice sera it is known that non-linear epitopes are recognized predominantly. Thus, it is contemplated that different forms of purification schemes known in the art will be used to analyze for the presence of discontinuous epitopes, and to analyze whether the human immune response is also directed against such epitopes.

Preferred embodiments of the present invention relate to species specific diagnostic tests according to the invention, wherein the nucleic acid fragments have sequences selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, and SEQ ID NO: 23.

In connection with nucleic acid fragments according to the

present invention the term "variant" should be understood as
a sequence of nucleic acids which shows a sequence homology
of less than 100%. A variant sequence can be of the same size
or it can be of a different size as the sequence it is
compared to. A variant will typically show a sequence
homology of at least 50%, preferably at least 60%, more
preferably at least 70%, such as at least 80%, e.g. at least
90%, 95% or 98%.

The term "sequence homology" in connection with nucleic acid fragments of the invention means the percentage of matching nucleic acids (with respect to both position and type) in the nucleic acid fragments of the invention and an aligned nucleic acid fragment of equal or different length.

In order to obtain information concerning the general distribution of each of the genes according to the present invention, PCR will be performed for each gene on all available *C. pneumoniae* isolates. This will provide information on the general variability of the genes or nucleic acid fragments of the invention. Variable regions will be sequenced. From patient samples PCR will be used to

amplify variable parts of the genes for epidemiology. Non-variable parts will be used for amplification by PCR and analyzed for possible use as a diagnostic test. It is contemplated that if variability is discovered, PCR of variable regions can be used for epidemiology. PCR of non-variable regions can be used as a species specific diagnostic test. Using genes encoding proteins known to be invariable in all known isolates prepared as targets for PCR to genes encoding proteins with unknown function.

- Particularly preferred embodiments of the present invention, relate to diagnostic tests according to the invention, wherein detection of nucleic acid fragments is obtained by using nucleic acid amplification, preferably polymerase chain reaction (PCR).
- Within the scope of the present invention is a PCR based test directed at detecting nucleic acid fragments of the invention or variants thereof. A PCR test will typically be developed according to methods well known in the art and will typically comprise a PCR test capable of detecting and differentiating between nucleic acid fragments of the invention. Preferred are quantitative competitive PCR tests or nested PCR tests. The PCR test according to the invention will typically be developed according to methods described in detail in EP B 540 588, EP A 586 112, EP A 643 140 OR EP A 669 401, which are hereby incorporated by reference.

Within the scope of the present invention are variants and subsequences of one of the nucleic acid fragments of the invention, meaning a consecutive stretch of nucleic acids taken from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23. A variant or subsequence will preferably comprise at least 100 nucleic acids, preferably at least 80 nucleic acids, more preferably at least 70 nucleic acids, such as at least 50 nucleic acids.

35 It might even be as small as 10-50 nucleic acids, such as

20-40 nucleic acids, e.g. about 30 nucleic acids. A subsequence will typically show a sequence homology of at least 30%, preferably at least 60%, more preferably at least 70%, such as at least 80%, e.g. at least 90%, 95% or 98%. The shorter the subsequence, the higher the required homology. Accordingly, a subsequence of 100 nucleic acids or lower must show a homology of at least 80%.

A very important aspect of the present invention relates to proteins of the invention derived from Chlamydia pneumoniae

10 having amino acid sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24 having a sequence similarity of at least 50%, preferably at least 60%, more preferably at least 70%, such as at least 80%, e.g. at least 90%, 95% or 98% and a similar biological function.

By the term "similar biological function" is meant that the protein shows characteristics similar with the proteins

20 derivable from the membrane proteins of Chlamydia pneumoniae.

Such proteins comprise repeated motifs of GGAI (at least 2, preferable at least 3 repeats) and/or conserved positions of tryptophan, (w).

Comparison of the DNA sequences from genes encoding Omp4-15
shows that the overall similarity between the individual
genes ranges between 43-55%. Comparison of the amino acid
sequences of Omp4-15 shows 34-49% identity and 53-64%
similarity. The homology is generally scattered along the
entire length of the deduced amino acids. However, as seen
from figure 8 A - J there are some regions in which the
homology is more pronounced. This is seen in the repeated
sequence where the sequence GGAI is repeated 4-7 times in the
genes. It is interesting that the DNA homology is not
conserved for the sequences encoding the four amino acids
GGAI. This may indicate a functional role of this part of the

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protein and indicates that the repeated structure did not occur by a duplication of the gene. In addition to the four amino acid repeats GGAI a region from amino acid 400 to 490 has a higher degree of homology than the rest of the protein, 5 with the conserved sequence FYDPI occurring in all sequences. As further indication of similarity in function the amino acid tryptophan (W) is perfectly conserved at 4-6 localizations in the C-terminal part of the protein.

Since none of the genes and deduced amino acid sequences of 10 the invention are identical the following is within the scope of the present invention; production of monospecific antibodies, the use of said antibodies for characterizing which C. pneumoniae proteins are expressed, the use of said antibodies for characterizing at which time during developmental life cycle said C. pneumoniae proteins are 15 expressed, and the use of said antibodies for characterizing the precise cellular localization of said C. pneumoniae proteins. Also within the scope of the present invention is the use of monospecific antibodies against proteins of the invention for determining which part of said proteins is 20 surface exposed and how proteins in the C. pneumoniae COMC interact with each other

Preferred embodiments of the present invention relate to polypeptides which comprise subsequences of the proteins of the invention, said subsequences comprising the sequence GGAI. Further preferred embodiments of the present invention relate to polypeptides which comprise subsequences of the proteins of the invention, said subsequences comprising the 30 sequence FSGE.

Polypeptides according to the invention will typically be of a length of at least 6 amino acids, preferably at least 15 amino acids, preferably at least 20 amino acids, preferably at least 25 amino acids, preferably at least 30 amino acids, preferably at least 35 amino acids, preferably at least 40 amino acids, preferably at least 45 amino acids, preferably

at least 50 amino acids, preferably at least 55 amino acids, preferably at least 100 amino acids.

A very important aspect of the present invention relates to nucleic acid fragments of the invention derived from Chlamydia pneumoniae, variants and subsequences thereof.

Another important aspect of the present invention relates to antibodies against the proteins according to the invention, such antibodies including polyclonal monospecific antibodies and monoclonal antibodies against proteins with sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24.

A very important aspect of the present invention relates to diagnostic kits for the diagnosis of infection of a mammal, such as a human, with *Chlamydia pneumoniae*, said kits comprising one or more proteins with amino acid sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24.

Another very important aspect of the present invention relates to diagnostic kits for the diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae, said kits comprising antibodies against a protein with an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24.

O Antibodies included in a diagnostic kit according to the invention can be polyclonal or monoclonal or a mixture hereof. Still another very important aspect of the present invention relates to diagnostic kits for the diagnosis of infection of a mammal, such as a human, with *Chlamydia pneumoniae*, said kits comprising one or more nucleic acid fragments with sequences selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, and SEQ ID NO: 23.

An aspect of the present invention relates to a composition for immunizing a mammal, such as a human, against Chlamydia pneumoniae, said composition comprising one or more proteins with amino acid sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24.

An important role for the proteins of the invention in prevention of infection of a mammal, such as a human, with *C. pneumoniae* is expected. Thus proteins of the invention,

20 including variants and subsequences will be produced, typically by using recombinant techniques, and will then be used as an antigen in immunization of mammals, such as rabbits. Subsequently, the hyper immune sera obtained by the immunization will be analyzed for protection against *C. pneumoniae* infection using a tissue culture assay. In addition it is contemplated that monoclonal antibodies will be produced, typically using standard hybridoma techniques, and analyzed for protection against infection with *C. pneumoniae*.

It is envisioned that particularly interesting and immunogenic epitopes will be found in connection with the proteins of the invention, which will comprise subsequences of said proteins. It is preferred to use polypeptides comprising such subsequences of the proteins of the invention

in immunizing a mammal, such as a human, against Chlamydia pneumoniae.

An important aspect of the present invention relates to the use of proteins with sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24 in diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae.

A preferred embodiment of the present invention relates to the use of proteins according to the invention in an undenatured form, in diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae.

A very important aspect of the present invention relates to the use of proteins with sequences selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, and SEQ ID NO: 24, for immunizing a mammal, such as a human, against Chlamydia pneumoniae.

A preferred embodiment of the present invention relates to the use of proteins according to the invention in an undenatured form, for immunizing a mammal, such as a human, against Chlamydia pneumoniae.

- A very important aspect of the present invention relates to the use of nucleic acid fragments with nucleotide sequences selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO:
- 30 19, SEQ ID NO: 21, and SEQ ID NO: 23 for immunizing a mammal, such as a human, against Chlamydia pneumoniae.

It is envisioned that one type of vaccine against *C*.

pneumoniae will be developed by using gene-gun vaccination of mice. Typically, different genetic constructs containing nucleic acid fragments, combinations of nucleic acid fragments according to the invention will be used in the gene-gun approach. The mice will then subsequently be analyzed for production of both humoral and cellular immune response and for protection against infection with *C*.

pneumoniae after challenge herewith.

In line with this, the invention also relates to the uses of the proteins of the invention as a pharmaceutical (a vaccine) as well as to the uses thereof for the preparation of a vaccine against infections with Chlamydia pneumoniae.

Preparation of vaccines which contain protein sequences as active ingredients is generally well understood in the art, 15 as exemplified by U.S. Patents 4,608,251; 4,601,903; 4,599,231; 4,599,230; 4,596,792; and 4,578,770, all incorporated herein by reference. Typically, such vaccines are prepared as injectables either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension 20 in, liquid prior to injection may also be prepared. The preparation may also be emulsified. The active immunogenic ingredient is often mixed with excipients which are pharmaceutically acceptable and compatible with the active ingred ent. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like, and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, or adjuvants which enhance the effectiveness of the vaccines. 30

The vaccines are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. These compositions take the form of

solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10-95% of active ingredient, preferably 25-70%, and optionally a suitable carrier.

The protein sequences may be formulated into the vaccine as neutral or salt forms known in the art. The vaccines are administered in a manner compatible with the dosage formulation, and in such amount as will be therapeutically effective and immunogenic. The quantity to be administered depends on the subject to be treated. Suitable dosage ranges 10 are of the order of several hundred micrograms active ingredient per vaccination with a preferred range from about 0.1 μg to 1000 μg . The immune response may be enhanced if the vaccine further comprises an adjuvant substance as known in 15 the art. Other possibilities involve the use of immunomodulating substances such as lymphokines (e.g. IFN- γ , IL-2 and IL-12) or synthetic IFN- γ inducers such as poly I:C in combination with the above-mentioned adjuvants.

It is also possible to produce a living vaccine by introducing, into a non-pathogenic microorganism, at least one
nucleic acid fragment encoding a protein fragment or protein
of the invention, and effecting expression of the protein
fragment or the protein on the surface of the microorganism
(e.g. in the form of a fusion protein including a membrane
anchoring part or in the form of a slightly modified protein
or protein fragment carrying a lipidation signal which allows
anchoring in the membrane). The skilled person will know how
to adapt relevant expression systems for this purpose.

Another part of the invention is based on the fact that

recent research have revealed that a DNA fragment cloned in a vector which is non-replicative in eukaryotic cells may be introduced into an animal (including a human being) by e.g. intramuscular injection or percutaneous administration (the so-called "gene gun" approach). The DNA is taken up by e.g.

muscle cells and the gene of interest is expressed by a

promoter which is functioning in eukaryotes, e.g. a viral promoter, and the gene product thereafter stimulates the immune system. These newly discovered methods are reviewed in Ulmer et al., 1993, which hereby is included by reference.

5 Thus, a nucleic acid fragment encoding a protein or protein of the invention may be used for effecting in vivo expression of antigens, i.e. the nucleic acid fragments may be used in so-called DNA vaccines. Hence, the invention also relates to a vaccine comprising a nucleic acid fragment encoding a protein fragment or a protein of the invention, the vaccine effecting in vivo expression of antigen by an mammal, such as a human, to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with 15 Chlamydia pneumoniae in an mammal, such as a human.

The efficacy of such a "DNA vaccine" can possibly be enhanced by administering the gene encoding the expression product together with a DNA fragment encoding a protein which has the capability of modulating an immune response. For instance, a gene encoding lymphokine precursors or lymphokines (e.g. IFN-20 γ , IL-2, or IL-12) could be administered together with the gene encoding the immunogenic protein fragment or protein, either by administering two separate DNA fragments or by administering both DNA fragments included in the same vector It is also a possibility to administer DNA fragments compri-25 sing a multitude of nucleotide sequences which each encode relevant epitopes of the protein fragments and proteins disclosed herein so as to effect a continuous sensitization of the immune system with a broad spectrum of these epitopes.

The following experimental non-limiting examples are intended to illustrate certain features and embodiments of the invention.

LEGENDS TO FIGURES

- Figure 1. The figure shows electron microscopy of negative stained purified C. pneumoniae EB (A) and purified OMC (B).
- Figure 2. The figure shows silver stained 15% SDS-PAGE of
 purified EB and OMC. Lane 1, purified C. pneumoniae EB; lane
 2, C. pneumoniae OMC; lane 3, purified C. trachomatis EB; and
 lane 4 C. trachomatis OMC.
- Figure 3. The figure shows immunoblotting of *C. pneumoniae* EB separated by 10% SDS-PAGE, transferred to nitrocellulose and reacted with rabbit anti *C. pneumoniae* OMC.
 - Figure 4. The figure shows coomassie blue stained 7.5% SDS-PAGE of recombinant pEX that were detected by the rabbit anti *C. pneumoniae* serum. Arrow indicated the localization of the 117 kDa b-galactosidase protein.
- 15 Figure 5. The figure shows immunoblotting of recombinant pEX colones detected by colony blotting separated by 7.5% SDS-PAGE and transferred to nitrocellulose and reacted with rabbit anti *C. pneumoniae* OMC. Lane 1, seablue molecular weight standard. Lane 2-6 pEX clones cultivated at 42°C to induce the production of the b-galactosidase fusion proteins.
 - Figure 6. The figure shows sequence strategy for Omp4 and Omp5. Arrows indicates primers used for sequencing.
- Figure 7. *C pneumoniae* omp genes. The genes are arranged in two clusters. In cluster 1 Omp12, 11, 10, 5, 4, 13, and 14 are found. In cluster 2 are found Omp6, 7, 8, 9, and 15.
 - Figure 8 A J. The figure shows alignment of C. pneumoniae Omp4-15, using the program pileup in the GCG package.
 - Figure 9. The figure shows immunofluorescence of *C*. pneumoniae infected HeLa, 72 hrs. after infection, reacted

with mouse monospecific anti-serum against pEX3-36 fusion protein. pEX3-36 is a part of the Omp5 gene.

Figure 10. The figure shows immunoblotting of *C. pneumoniae* EB, lane 1-3 heated to 100°C in SDS-sample buffer, lane 4-6 unheated. Lane 1 reacted with rabbit anti *C. pneumoniae* OMC; lane 2 and 4 pre-serum; lane 3 and 5 polyclonal rabbit anti pEX1-1 fusion protein; lane 6 MAb 26.1.

Figure 11. The figure shows immunoblotting of *C. pneumoniae* EB, lane 1-4 heated to 100oC in SDS-sample buffer, lane 5-6 unheated. Reacted with serum from C57-black mice 14 days after infection with 10⁷ CFU of *C. pneumoniae*. Lane 1 and 5 mouse 1; lane 2 and 6 mouse 2; lane 3 and 5 mouse 3; and lane 4 and 8 mouse 4.

Figure 12. The figure shows immunohistochemistry analysis of mouse lung tissue with *C. pneumoniae* inclusions present both in the bronchial epithelium and in the lung parenchyma (arrows).

EXAMPLE 1

Cloning of the genes encoding the 98/95 kDa C. pneumoniae COMC proteins

Purification of C. pneumonia EBs and COMC

- C. pneumoniae was cultivated in HeLa cells. Cultivation was done according to the specifications of Miyashita and Matsumoto (1992), with the modification that centrifugation of supernatant and of the later precipitate and turbid bottom layer was carried out at 100,000 X g. The microorganism attached to the HeLa cells by 30 minutes of centrifugation at 10 1000 x g, after which the cells were incubated in RPMI 1640 medium (Gibco BRL, Germany cat No. 51800-27), containing 5% foetal calf serum (FCS, Gibco BRL, Germany Cat No. 10106.169) gentamicin for two hours at 37°C in 5% CO2 atmosphere. The medium was changed to medium that in addition contained 1 mg 15 per ml of cycloheximide. After 48 hours of incubation a coverslip was removed from the cultures and the inclusion was tested with an antibody specific for C. pneumoniae (MAb 26.1) (Christiansen et al. 1994) and a monoclonal antibody specific for the species C. trachomatis (MAb 32.3, Loke diagnostics, 20 Århus Denmark) to ensure that no contamination with C. trachomatis had occurred. The HeLa cells were tested by Hoechst stain for Mycoplasma contamination as well as by culture in BEa and BEg medium (Freund et al., 1979). Also the C. pneumoniae stocks were also tested for Mycoplasma contamination by cultivation in BEa and BEg medium. No contamination with C. trachomatis, Mycoplasmas or bacteria were detected in cultures or cells. 72 hours post-infection
- 25 the monolayer was washed in PBS, the cells were loosened in
- PBS with a rubber policeman, and the Chlamydia were liberated from the host cell by sonication. The C. pneumoniae EBs and RBs were purified on discontinuous density gradients (Miyashita et al. (1992)). The purity of the Chlamydia EBs were verified by negative staining and electronmicroscopy
- (Figure 1), only particles of a size of 0.3 to 0.5 mm were 35

detected in agreement with the structure of *C. pneumonia* EBs. The purified Chlamydia EBs were subjected to sarkosyl extraction as described by Caldwell et al (1981) with the modification that a brief sonication was used to suspend the COMC. The purified COMC was tested by electronmicroscopy and negative staining (Figure 1), where a folded outer membrane complex was seen.

SDS-PAGE analysis of purified EBs and COMC

The proteins from purified EBs and C. pneumoniae OMC were separated on 15% SDS-polyacrylamide gel, and the gel was 10 silver stained (Figure 2), in lane 1 it is seen that the purified EBs contain major proteins of 100/95 kDa and a protein of 38 kDa, in the purified COMC (lane 2) these two protein groups are also dominant. In addition, proteins with a molecular weight of $62/60~\mathrm{kDa}$, 55 kDa, and 12 kDa have been 15 enriched in the COMC preparation. When the purified C. pneumoniae EBs are compared to purified C. trachomatis EB (lane 3) it is seen that predominant protein in the C. trachomatis EB is the major outer membrane protein (MOMP), and it is also the dominant band in the COMC preparation of 20 C. trachomatis (lane 4), and Omp2 of 60/62 kDa as well as Omp3 at 12 kDa are seen in the preparation. However, no major bands with a size of 100/95 kDa are detected as in the C. pneumoniae COMC preparation.

25 Production of rabbit polyclonal antibodies against C. pneumoniae COMC

To ensure production of rabbit antibodies that would recognize all the C. pneumoniae proteins in immuno-blotting and colony-blotting 10 μg of COMC antigen was dissolved in 20 μl of SDS sample buffer and thereafter divided into 5 vials. The dissolved antigen was further diluted in one ml of PBS and one ml of Freund incomplete adjuvant (Difco laboratories, USA cat. No. 0639-60-6) and injected into the quadriceps muscle of a New Zealand white rabbit. The rabbit was given

three times intramuscular injections at an interval of one week, and after further three weeks the dissolved COMC protein, diluted in one ml PBS was injected intravenously, and the procedure was repeated two weeks later. Eleven weeks after the beginning of the immunization, the serum was obtained from the rabbit. Purified *C. pneumoniae* EBs were separated by SDS-PAGE, and the proteins were electrotransferred to nitrocellulose membrane. The membrane was blocked and immunostained with the polyclonal COMC antibody (Figure 3). The serum recognized proteins with a size of 100/95, 60 and 38 kDa in the EB preparation. This is in agreement with the sizes of the outer membrane proteins.

Cloning of the COMC proteins

Due to the cultivation of C. pneumoniae in HeLa cells, contaminating host cell DNA could be present in the EB 15 preparations. Therefore, the purified EB preparations were treated with DNAse to remove contaminating DNA. The C. pneumoniae DNA was then purified by CsCl gradient centrifugation. The C. pneumoniae DNA was partially digested with Sau3A and the fractions containing DNA fragments with a 20 size of approx. 0.5 to 4.0 kb were cloned into the expression vector system pEX (Boehringer, Germany cat. No. 1034 766, 1034 774, 1034 782). The pEX vector system has a eta-galactosidase gene with multiple cloning sites in the 3'end of the β -galactosidase gene. Expression of the gene is regulated by the PR promoter, so the protein expression can be induced by elevating the temperature from 32 to 42°C . The colonies of recombinant bacteria were transferred to nitrocellulose membranes, and the temperature was increased to 42°C for two hours. The bacteria were lysed by placing the 30 nitrocellulose membranes on filters soaked in 5% SDS. The colonies expressing outer membrane proteins were detected with the polyclonal antibody raised against C. pneumoniae COMC. The positive clones were cultivated in suspension and induced at 42°C for two hours. The protein profile of the 35 clones were analysed by SDS-PAGE, and increases in the size

of the induced b-galactosidase were observed (Figure 4). In addition, the proteins were electrotransferred to nitrocellulose membranes, and the reaction with the polyclonal serum against COMC was confirmed (Figure 5).

5 Sequencing of positive COMC clones

To characterize the pEX clones, the inserted C. pneumoniae DNA was sequenced. The resulting DNA sequences were searched against the prokaryotic sequences in the GenEmbl database. The search identified 6 clones as part of the Omp2 gene, and 2 clones as part of the Omp3 gene, and 2 clones as part of 10 the MOMP gene, indicating that COMC proteins had been successfully cloned. Furthermore, 32 clones were obtained, containing DNA sequences not found in the GenEmbl database. These sequences could, however, be clustered in two contics of 6 and 4 clones, and three clones were identical. In 15 addition 19 clones were found with no overlap to the contics (Figure 7). To obtain more sequence data for the genes, C. pneumoniae DNA was totally digested with BamHI restriction enzyme, and the fragments were cloned into the vector 20 pBluescript. The ligated DNA was electrotransformed into E. coli XL1-Blue and selected on plates containing Ampicillin. The recombinant bacterial colonies were transferred to a nitrocellulose membrane, and colony hybridisation was performed using the inserts of pEX 1-1 clone as a probe. A clone containing a single BamHI fragment of 4.5 kb was found, 25 and the hybridisation to the probe was confirmed by Southern blotting. The insert of the clone was sequenced bi-directionally using synthetic primers for approx. each 300 bp. The sequence of the BamHI fragment made it possible to join the two contics of pEX clones. Totally, together with 30 the pEX clones it was possible to assemble 6.5 kb DNA sequence, encoding two new COMC proteins. (Figure 6)

Additional sequences were obtained by PCR performed on purified *C. pneumoniae* DNA with primers both from the known Omp genes and from other known genes. The obtained PCR

products were sequenced, The sequence organisation is shown in Fig. 7. Additional 8 Omp genes were detected. The alignment of the deduced amino acid sequences are shown in Fig. 8 A and B.

Analysis of DNA sequence

The DNA sequence encoding the Omp4-15 proteins with a size of 89.6-100.3 kDa (and for Omp13: 56.1 kDa). Omp4 and Omp5 were transcribed in opposite directions. Downstream Omp4 a possible termination structure was located. The 3'end of the 10 Omp5 gene was not cloned due to the presence of the BamHI restriction enzyme site positioned within the gene. The translated DNA sequence of Omp4 and Omp5 was compared by use of the gap programme in the GCG package (Wisconsin package, version 8.1-UNIX, August 1995, sequence analysis software package). The two genes had an amino acid identity of 41% 15 (similarity 61%), and a possible cleavage site for signal peptidase 1 was present at amino acid 17 in Omp4 and amino acid 25 in Omp5. When the amino acid sequence encoded by two other pEX clones were compared to the sequence of Omp4 and 20 Omp5 they also had amino acid homology to the genes. It is seen that the two clones have homology to the same area in the Omp4 and Omp5 proteins. Consequently, the pEX clones must have originated from two additional genes. Therefore these genes were named Omp6 and Omp7. Similar analyses were performed with the other genes. In contrast to what was seen 25 for Omp4 and 5 none of the other putative omp proteins had a cleavage site for signal peptides.

EXAMPLE 2

Polyclonal monospecific antibodies against pEX fusion proteins and full length recombination + Omp4

To investigate the topology of the Omp4-7 proteins, representative pEX clones, were selected from each gene. The fusion proteins of β -galactosidase/omp were induced, and the

proteins were partially purified as inclusion bodies. Balb/c mice were immunized three times intramuscular with the antigens at an interval of one week, and after six weeks the serum was obtained from the mice. HeLa cells were infected with the C. pneumoniae. 72 hours after the infection the mono-layers were fixed with 3.7% formaldehyde. This treatment makes the outer membrane of the Chlamydia impermeable for antibodies due to the extensive cross-linking of the outer membrane proteins by the formaldehyde. The HeLa cells were permeabilized with 0.2% Triton X100, the monolayers were 10 washed in PBS, then incubated with 20% (v/v) FCS to inactivate free radicals of the formaldehyde. The mice sera were diluted 1:100 PBS with 20% (v/v) FCS and incubated with the monolayers for half an hour. The monolayers were washed in PBS and secondary FITCH conjugated rabbit anti mouse serum 15 was added for half an hour, and the monolayers were washed and mounted. Several of the antibodies reacted strongly with the EBs in the inclusions (Figure 9). In spite of the formaldehyde fixation it could not be excluded that the surface of the EB was changed by the treatments, so that the 20 antibodies could get access to the Omp4-7. Therefore, the reaction was confirmed by immuno-electron microscopy with the antibody raised against clone pEX3-36. Purified EB of C. pneumoniae were absorbed to carbon coated nickel grids. After the absorption the grids were washed with PBS and blocked in 25 0.5% Ovalbumin dissolved in PBS. The antibodies were diluted 1:100 in the same buffer and incubated for 30 minutes. The grids were washed in PBS. Rabbit anti mouse Ig conjugated with 10nm colloidal gold diluted in PBS containing 1% gelatin was added to the grids for half an hour. The grids were 30 washed in 3 \times PBS with 1% gelatin and 3 times in PBS, the grids were contrastained with 0.7% phospho tungstic acid. The grids were analysed in a Jeol 1010 electron microscope at 40 kV. It was seen that the gold particles were covering the surface of the purified EB. Because the C. pneumoniae EBs 35 were not exposed to any detergent or fixation under either the purification or the reaction with antibodies, these

results show that the cloned proteins have surface exposed epitopes.

Polyclonal monospecific antibodies against Omp4

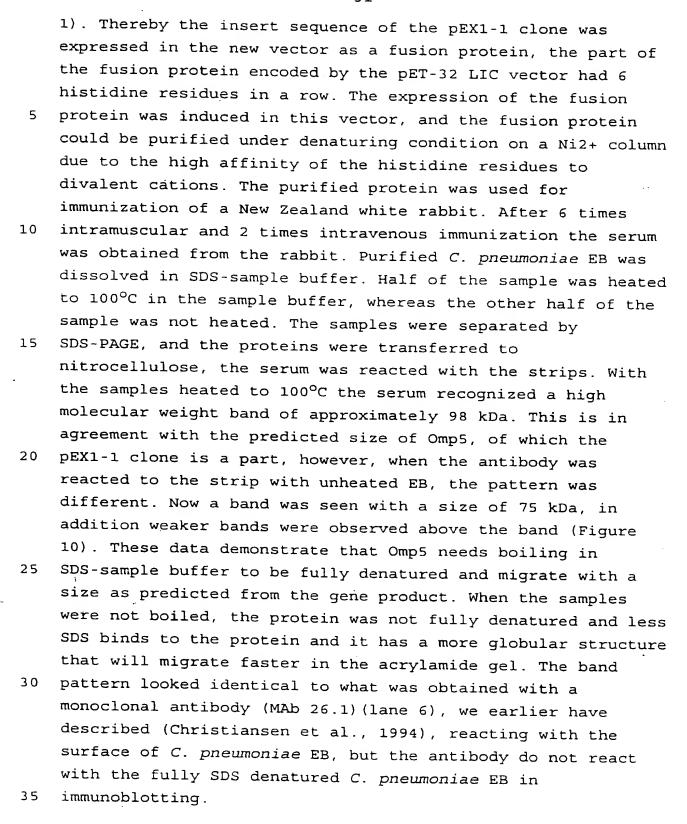
The Omp4 gene was amplified by PCR with primers that contained LIC-sites, and the PCR product was cloned into the pET-30 LIC vector (Novagen). The histidine tagged fusion protein was expressed by induction of the synthesis by IPTG and purified over a nickel column. The purified Omp4 protein was used for immunization of a rabbit (six times, 8 μ g each time).

Use of rabbit polyclonal antibodies to recombinant Omp4 for detection of *Chlamydia pneumoniae* in paraffin embedded sections

The lungs of C. pneumoniae infected mice were obtained three days after intranasal infection. The tissue samples were 15 fixed in 4% formaldehyde, paraffin embedded, sectioned and deparaffinized prior to staining. The sections were incubated with the rabbit serum diluted 1:200 in TBS (150 mM NaCl, 20mM Tris pH 7.5) for 30 min at room temperature. After wash two times in TBS the sections were incubated with the 20 secondary antibody (biotinylated goat anti-rabbit antibodies) diluted 1:300 in TBS, followed by two times wash in TBS. The sections were stained with streptavidin-biotin complex (streptABComplex/AP, Dako) for 30 min washed and developed under microscopic inspection with chromagen + new fuchsin 25 (Vector laboratories). The sections were counter stained with Hematoxylin and analyzed ny microscopy.

Immuno blotting analysis with hyperimmune monospecific rabbit anti-serum

The insert of pEX1-1 clone was amplified by PCR using primers containing LIC sites. The PCR product could therefore be inserted in the pET-32 LIC vector (Novagen, UK cat No. 69076-



Experimental infection of C57 black mice

Due to the realization of the altered migration of the Omp4-7 proteins without boiling, we chose to analyse antibodies against C. pneumoniae EBs after an experimental infection of mice. To obtain antibodies from an infection caused by C. pneumoniae, C57 black mice were inoculated intranasally with 10^7 CFI of C. pneumoniae under a light ether anaesthesia. After 14 days of infection the serum samples were obtained and the lungs were analysed for pathological changes. In two of the mice a severe pneumonia was observed in the lung sections, and in the third mouse only minor changes were observed. The serum from the mice was diluted 1:100 and reacted with purified EBs dissolved in sample buffer with and without boiling. In the preparations that had been heated to 100°C the sera from two of the mice reacted strongly with 15 bands of 60/62 kDa and weaker bands of 55 kDa, but no reaction was observed with proteins of the size of Omp4-7 (Figure 11). However, when the sera were reacted with the preparation that had not been heated they all had a strong reaction with a broad band of an approximate size of 75 kDa. 20 This is in agreement with the size of the Omp4-7 proteins in the unheated preparation. Therefore, it could be concluded that the epitopes of the Omp4-7 proteins recognized by the antibodies after a C. pneumoniae infection were discontinuous epitopes because the full denaturation of the antigen 25 completely destroyed the epitopes. The 75 kDa protein observed in unheated samples is not Omp2 (Shown in immunoblotting with an Omp2 specific antibody)

EXAMPLE 3

Comparison of Omp4-7 of *C. pneumoniae* with putative outer membrane proteins (POMP) of *C. psittaci*

Longbottom et al. (1996) have published partial sequence from 98 to 90 kDa proteins from *C. psittaci*. They have entered the full sequence of 5 genes in this family in the EMBL database.

They have named the genes "putative outer membrane proteins" (POMP) since their precise location was not determined. The family is composed of two genes that are completely identical, and two genes with high homology to these genes. They calculated a molecular size of 90 and 91 kDa. The 5th encode a protein of 98 kDa. The sequence of the Omp4-7 proteins of C. pneumoniae were compared to the sequences of the C. Psittaci POMP proteins with the programme pileup in the GCG package. The amino acid homologies were in the range of 51-63%. It is seen that the C. pneumoniae Omp4-5 proteins 10 are most related to the 98 kDa POMP protein of C. psittaci. Interestingly, the 98 kDa C. psittaci POMP protein is more related to the C. pneumoniae genes than to the other C. psittaci genes. The repeated sequences of GGAI were conserved in the 98 kDa POMP protein, but only three GGAI repeats were 15 present in the 90 and 91 kDa C. psittaci POMP proteins. For

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SEQUENCE LISTING

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- (E) COUNTRY: Denmark
- (F) POSTAL CODE: 8000
- (ii) TITLE OF THE INVENTION: Chlamydia pneumoniae anti
- (iii) NUMBER OF SEQUENCES: 30
- (iv) COMPUTER-READABLE FORM:
 - (A) MEDIUM TYPE: Diskette
 - (B) COMPUTER: IBM Compatible
 - (C) OPERATING SYSTEM: DOS
 - (D) SOFTWARE: FastSEQ for Windows Version 2.0
- (v) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (2) INFORMATION FOR SEQ ID NO:1:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3200 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 205...2987
 - (D) OTHER INFORMATION:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

CAATGTCGAA GAGAGCACTA ACCAGGAAAA TTGCGATTTC ATAAACCCAC TTTATTATTA 60
AATTCTTACT TGCGTCATAT AAAATAGAAA ACTCAGAGAG TCAAGATAAA AATTCTTGAC 120
AGCTGTTTTG TCATCTTTAA CTTGATTTAC TTATTTTGTT TCTATATTGA TGCGAATAGT 180
TCTCTAAAAA ACAAAAGCAT TACC ATG AAG ACT TCG ATT CCT TGG GTT TTA 231

Met Lys Thr Ser Ile Pro Trp Val Leu

GTT TCC TCC GTG TTA GCT TTC TCA TGT CAC CTA CAG TCA CTA GCT AAC
Val Ser Ser Val Leu Ala Phe Ser Cys His Leu Gln Ser Leu Ala Asn
10 20 25

GAG Glu	GAA Glu	CTT Leu	TTA Leu	TCA Ser 30	CCT Pro	GAT Asp	GAT Asp	AGC Ser	TTT Phe 35	AAT Asn	GGA Gly	AAT Asn	ATC Ile	GAT Asp 40	TCA Ser		327
GGA Gly	ACG Thr	TTT Phe	ACT Thr 45	CCA Pro	AAA Lys	ACT Thr	TCA Ser	GCC Ala 50	ACA Thr	ACA Thr	TAT Tyr	TCT Ser	CTA Leu 55	ACA Thr	GGA Gly		375
GAT Asp	GTC Val	TTC Phe 60	TTT Phe	TAC Tyr	GAG Glu	CCT Pro	GGA Gly 65	AAA Lys	GGC Gly	ACT Thr	CCC Pro	TTA Leu 70	TCT Ser	GAC Asp	AGT Ser		423
TGT Cys	TTT Phe 75	AAG Lys	CAA Gln	ACC Thr	ACG Thr	GAC Asp 80	AAT Asn	CTT Leu	ACC Thr	TTC Phe	TTG Leu 85	GGG Gly	AAC Asn	GGT Gly	CAT His		471
AGC Ser 90	TTA Leu	ACG Thr	TTT Phe	GGC Gly	TTT Phe 95	ATA Ile	GAT Asp	GCT Ala	GGC Gly	ACT Thr 100	CAT His	GCA Ala	GGT Gly	GCT Ala	GCT Ala 105		519
GCA Ala	TCT Ser	ACA Thr	ACA Thr	GCA Ala 110	AAT Asn	AAG Lys	AAT Asn	CTT Leu	ACC Thr 115	TTC Phe	TCA Ser	GGG Gly	TTT Phe	TCC Ser 120	TTA Leu	/	567
CTG Leu	AGT Ser	TTT Phe	GAT Asp 125	TCC Ser	TCT Ser	CCT Pro	AGC Ser	ACA Thr 130	ACG Thr	GTT Val	ACT Thr	ACA Thr	GGT Gly 135	CAG Gln	GGA Gly		615
ACG Thr	CTT Leu	TCC Ser 140	TCA Ser	GCA Ala	GGA Gly	GGC Gly	GTA Val 145	AAT Asn	TTA Leu	GAA Glu	AAT Asn	ATT Ile 150	CGT Arg	AAA Lys	CTT Leu		663
GTA Val	GTT Val 155	GCT Ala	GGG Gly	AAT Asn	TTT Phe	TCT Ser 160	ACT Thr	GCA Ala	GAT Asp	GGT	GGA Gly 165	GCT Ala	ATC Ile	AAA Lys	GGA Gly		711
GCG Ala 170	TCT Ser	TTC Phe	CTT Leu	TTA Leu	ACT Thr 175	GGC Gly	ACT Thr	TCT Ser	GGA Gly	GAT Asp 180	GCT Ala	CTT Leu	TTT Phe	AGT Ser	AAC Asn 185		759
AAC Asn	TCT	TCA Ser	TCA Ser	ACA Thr 190	AAG Lys	GGA Gly	GGA Gly	GCA Ala	ATT Ile 195	GCT Ala	ACT Thr	ACA Thr	GCA Ala	GGC Gly 200	GCT Ala		807
CGC Arg	ATA Ile	GCA Ala	AAT Asn 205	AAC Asn	ACA Thr	GGT Gly	TAT Tyr	GTT Val 210	AGA Arg	TTC Phe	CTA Leu	TCT Ser	AAC Asn 215	ATA Ile	GCG Ala		855
TCT Ser	ACG Thr	TCA Ser 220	Gly	GGC Gly	GCT Ala	ATC	GAT Asp 225	Asp	GAA Glu	GGC Gly	ACG Thr	TCG Ser 230	ATA Ile	CTA Leu	TCG Ser		903
AAC Asn	AAC Asn 235	Lys	TTT Phe	CTA Leu	TAT	TTT Phe 240	Glu	. GGG . Gly	AAT Asn	GCA Ala	GCG Ala 245	Lys	ACT Thr	ACT Thr	GGC Gly		951
GGT	GCG	ATC	TGC	AAC	ACC	: AAG	GCG	AGT	' GGA	TCT	CCT	GAA	CTG	ATA	ATC		999

Gly 250	Ala	Ile	Cys	Asn	Thr 255	Lys	Ala	Ser	Gly	Ser 260	Pro	Glu	Leu	Ile	Ile 265	
TCT Ser	AAC Asn	AAT Asn	AAG Lys	ACT Thr 270	CTG Leu	ATC Ile	TTT Phe	GCT Ala	TCA Ser 275	AAC Asn	GTA Val	GCA Ala	GAA Glu	ACA Thr 280	AGC Ser	1047
GGT Gly	GGC Gly	GCC Ala	ATC Ile 285	CAT His	GCT Ala	AAA Lys	AAG Lys	CTA Leu 290	GCC Ala	CTT Leu	TCC Ser	TCT Ser	GGA Gly 295	GGC Gly	TTT Phe	1095
ACA Thr	GAG Glu	TTT Phe 300	CTA Leu	CGA Arg	AAT Asn	AAT Asn	GTC Val 305	TCA Ser	TCA Ser	GCA Ala	ACT Thr	CCT Pro 310	AAG Lys	GGG Gly	GGT Gly	1143
GCT Ala	ATC Ile 315	AGC Ser	ATC Ile	GAT Asp	GCC Ala	TCA Ser 320	GGA Gly	GAG Glu	CTC Leu	AGT Ser	CTT Leu 325	TCT Ser	GCA Ala	GAG Glu	ACA Thr	1191
GGA Gly 330	AAC Asn	ATT Ile	ACC Thr	TTT Phe	GTA Val 335	AGA Arg	AAT Asn	ACC Thr	CTT Leu	ACA Thr 340	ACA Thr	ACC Thr	GGA Gly	AGT Ser	ACC Thr 345	1239
GAT Asp	ACT Thr	CCT Pro	AAA Lys	CGT Arg 350	AAT Asn	GCG Ala	ATC Ile	AAC Asn	ATA Ile 355	GGA Gly	AGT Ser	AAC Asn	GGG Gly	AAA Lys 360	TTC Phe	1287
ACG Thr	GAA Glu	TTA Leu	CGG Arg 365	GCT Ala	GCT Ala	AAA Lys	AAT Asn	CAT His 370	ACA Thr	ATT Ile	TTC Phe	TTC Phe	TAT Tyr 375	GAT Asp	CCC Pro	1335
ATC Ile	ACT Thr	TCA Ser 380	GAA Glu	GGA Gly	ACC Thr	TCA Ser	TCA Ser 385	GAC Asp	GTA Val	TTG Leu	AAG Lys	ATA Ile 390	AAT Asn	AAC Asn	GGC Gly	1383
TCT Ser	GCG Ala 395	GGA Gly	GCT Ala	CTC Leu	AAT Asn	CCA Pro 400	TAT Tyr	CAA Gln	GGA Gly	ACG Thr	ATT Ile 405	CTA Leu	TTT Phe	TCT Ser	GGA Gly	1431
GAA Glu 410	ACC Thr	CTA Leu	ACA Thr	GCA Ala	GAT Asp 415	GAA Glu	CTT Leu	AAA Lys	GTT Val	GCT Ala 420	GAC Asp	AAT Asn	TTA Leu	AAA Lys	TCT Ser 425	1479
TCA Ser	TTC Phe	ACG Thr	CAG Gln	CCA Pro 430	GTC Val	TCC Ser	CTA Leu	TCC Ser	GGA Gly 435	GGA Gly	AAG Lys	TTA Leu	TTG Leu	CTA Leu 440	CAA Gln	1527
AAG Lys	GGA Gly	GTC Val	ACT Thr 445	TTA Leu	GAG Glu	AGC Ser	ACG Thr	AGC Ser 450	TTC Phe	TCT Ser	CAA Gln	GAG Glu	GCC Ala 455	GGT Gly	TCT Ser	1575
CTC Leu	CTC Leu	GGC Gly 460	ATG Met	GAT Asp	TCA Ser	GGA Gly	ACG Thr 465	ACA Thr	TTA Leu	TCA Ser	ACT Thr	ACA Thr 470	GCT Ala	GGG Gly	AGT Ser	1623
ATT Ile	ACA Thr	ATC Ile	ACG Thr	AAC Asn	CTA Leu	GGA Gly	ATC Ile	AAT Asn	GTT Val	GAC Asp	TCC Ser	TTA Leu	GGT Gly	CTT Leu	AAG Lys	1671

38

	475					480					485					
CAG Gln 490	CCC Pro	GTC Val	AGC Ser	CTA Leu	ACA Thr 495	GCA Ala	AAA Lys	GGT Gly	GCT Ala	TCA Ser 500	AAT Asn	AAA Lys	GTG Val	ATC Ile	GTA Val 505	1719
TCT Ser	GGG Gly	AAG Lys	CTC Leu	AAC Asn 510	CTG Leu	ATT Ile	GAT Asp	ATT Ile	GAA Glu 515	GGG Gly	AAC Asn	ATT Ile	TAT Tyr	GAA Glu 520	AGT Ser	1767
CAT His	ATG Met	TTC Phe	AGC Ser 525	CAT His	GAC Asp	CAG Gln	CTC Leu	TTC Phe 530	TCT Ser	CTA Leu	TTA Leu	AAA Lys	ATC Ile 535	ACG Thr	GTT Val	1815
GAT Asp	GCT Ala	GAT Asp 540	GTT Val	GAT Asp	ACT Thr	AAC Asn	GTT Val 545	GAC Asp	ATC Ile	AGC Ser	AGC Ser	CTT Leu 550	ATC Ile	CCT Pro	GTT Val	1863
CCT Pro	GCT Ala 555	GAG Glu	GAT Asp	CCT Pro	AAT Asn	TCA Ser 560	GAA Glu	TAC Tyr	GGA Gly	TTC Phe	CAA Gln 565	GGA Gly	CAA Gln	TGG Trp	AAT Asn	1911
GTT Val 570	AAT Asn	TGG Trp	ACT Thr	ACG Thr	GAT Asp 575	ACA Thr	GCT Ala	ACA Thr	AAT Asn	ACA Thr 580	AAA Lys	GAG Glu	GCC Ala	ACG Thr	GCA Ala 585	1959
ACT Thr	TGG Trp	ACC Thr	AAA Lys	ACA Thr 590	GGA Gly	TTT Phe	GTT Val	CCC Pro	AGC Ser 595	CCC Pro	GAA Glu	AGA Arg	AAA Lys	TCT Ser 600	GCG Ala	2007
TTA Leu	GTA Val	TGC Cys	AAT Asn 605	ACC Thr	CTA Leu	TGG Trp	GGA Gly	GTC Val 610	TTT Phe	ACT Thr	GAC Asp	ATT Ile	CGC Arg 615	TCT Ser	CTG Leu	2055
CAA Gln	CAG Gln	CTT Leu 620	GTA Val	GAG Glu	ATC Ile	GGC Gly	GCA Ala 625	ACT Thr	GGT Gly	ATG Met	GAA Glu	CAC His 630	AAA Lys	CAA Gln	GGT Gly	2103
TTC Phe	TGG Trp 635	GTT Val	TCC Ser	TCC Ser	ATG Met	ACG Thr 640	AAC Asn	TTC Phe	CTG Leu	CAT His	AAG Lys 645	ACT Thr	GGA Gly	GAT Asp	GAA Glu	2151
AAT Asn 650	CGC Arg	AAA Lys	GGC Gly	TTC Phe	CGT Arg 655	CAT His	ACC Thr	TCT Ser	GGA Gly	GGC Gly 660	TAC Tyr	GTC Val	ATC Ile	GGT Gly	GGA Gly 665	2199
AGT Ser	GCT Ala	CAC His	ACT Thr	CCT Pro 670	AAA Lys	GAC Asp	GAC Asp	CTA Leu	TTT Phe 675	ACC Thr	TTT Phe	GCG Ala	TTC Phe	TGC Cys 680	CAT His	2247
CTC Leu	TTT Phe	GCT Ala	AGA Arg 685	GAC Asp	AAA Lys	GAT Asp	TGT Cys	TTT Phe 690	ATC Ile	GCT Ala	CAC His	AAC Asn	AAC Asn 695	TCT Ser	AGA Arg	2295
ACC Thr	TAC Tyr	GGT Gly 700	GGA Gly	ACT Thr	TTA Leu	TTC Phe	TTC Phe 705	AAG Lys	CAC His	TCT Ser	CAT His	ACC Thr 710	CTA Leu	CAA Gln	CCC Pro	2343

CAA Gln	AAC Asn 715	TAT	TTG Leu	AGA Arg	TTA Leu	GGA Gly 720	AGA Arg	GCA Ala	AAG Lys	TTT Phe	TCT Ser 725	GAA Glu	TCA Ser	GCT Ala	ATA Ile	2391
GAA Glu 730	AAA Lys	TTC Phe	CCT Pro	AGG Arg	GAA Glu 735	ATT Ile	CCC Pro	CTA Leu	GCC Ala	TTG Leu 740	GAT Asp	GTC Val	CAA Gln	GTT Val	TCG Ser 745	2439
TTC Phe	AGC Ser	CAT His	TCA Ser	GAC Asp 750	AAC Asn	CGT Arg	ATG Met	GAA Glu	ACG Thr 755	CAC His	TAT Tyr	ACC Thr	TCA Ser	TTG Leu 760	CCA Pro	2487
GAA Glu	TCC Ser	GAA Glu	GGT Gly 765	TCT Ser	TGG Trp	AGC Ser	AAC Asn	GAG Glu 770	TGT Cys	ATA Ile	GCT Ala	GGT Gly	GGT Gly 775	ATC Ile	GGC Gly	2535
CTA Leu	GAC Asp	CTT Leu 780	CCT Pro	TTT Phe	GTT Val	CTT Leu	TCC Ser 785	AAC Asn	CCA Pro	CAT His	CCT Pro	CTT Leu 790	TTC Phe	AAG Lys	ACC Thr	2583
TTC Phe	ATT Ile 795	CCA Pro	CAG Gln	ATG Met	AAA Lys	GTC Val 800	GAA Glu	ATG Met	GTT Val	TAT Tyr	GTA Val 805	TCA Ser	CAA Gln	AAT Asn	AGC Ser	2631
TTC Phe 810	TTC Phe	GAA Glu	AGC Ser	TCT Ser	AGT Ser 815	GAT Asp	GGC Gly	CGT Arg	GGT Gly	TTT Phe 820	AGT Ser	ATT Ile	GGA Gly	AGG Arg	CTG Leu 825	2679
CTT Leu	AAC Asn	CTC Leu	TCG Ser	ATT Ile 830	CCT Pro	GTG Val	GGT Gly	GCG Ala	AAA Lys 835	TTC Phe	GTG Val	CAG Gln	GGG Gly	GAT Asp 840	ATC Ile	2727
GGA Gly	GAT Asp	TCC Ser	TAC Tyr 845	Thr	TAT Tyr	GAT Asp	CTC Leu	TCA Ser 850	GGA Gly	TTC Phe	TTT Phe	GTT Val	TCC Ser 855	GAT Asp	GTC Val	2775
TAT Tyr	CGT Arg	AAC Asn 860	AAT Asn	CCC Pro	CAA Gln	TCT Ser	ACA Thr 865	GCG Ala	ACT Thr	CTT Leu	GTG Val	ATG Met 870	AGC Ser	CCA Pro	GAC Asp	2823
TCT Ser	TGG Trp 875	AAA Lys	ATT	CGC Arg	GGT Gly	GGC Gly 880	AAT Asn	CTT	TCA Ser	AGA Arg	CAG Gln 885	GCA Ala	TTT Phe	TTA Leu	CTG Leu	2871
AGG Arg 890	Gly	AGC Ser	AAC Asn	AAC Asn	TAC Tyr 895	GTC Val	TAC Tyr	AAC Asn	TCC Ser	AAT Asn 900	TGT Cys	GAG Glu	CTC Leu	TTC Phe	GGA Gly 905	2919
														GTA Val 920		2967
GTT Val	GGT Gly	ACC	AAA Lys 925	Leu	CGA Arg	TT Phe	CTAG	ATTG	CT A	AAAC	TCCC	T AG	TTCT	TCTA	GGGAG	3022
TTI	TCTC	ATA	CTTT	TAGG	GA A	ATAT	TTGC	T AT	AGGG	AATG	CTT	тсст	TGC	AAAC	TGTAAA	3082

AAATAACATT TGTCCCTCTT CAAAAAAGAT TTCTTTTAAT AATTTCTAGT TATAATTTTA 3142 TTTTTAAAAAC AGTTAAATAA TTAATAGACA ATAATCTATT CTTATTGACT TCTTTTTT 3200

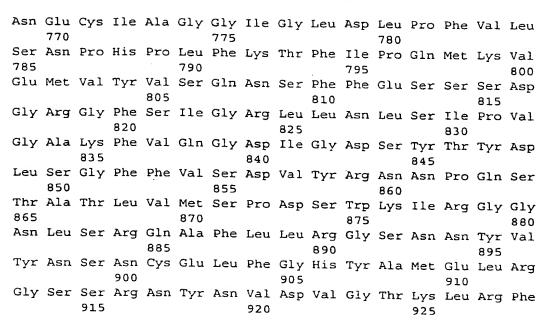
(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 928 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

	Τ.				5					10					Ala 15	
				20					25					3.0	Pro	
			35					40					45	Pro	Lys	
•		50					55					60			Glu	
	65					70					75				Thr	9.0
					85					90					Phe 95	
				T00					105					110	Asn	
			115					120					125		Ser	
		T30					135					140			Gly	
	142	1				150					155				Phe	1.00
					165					170					Thr	Gly
				180					185					190	Lys	
			T 3 2					200					205	Asn	Thr	
		210					215					220			Ala	
	225					230					235				Tyr	240
					245					250					Thr 255	Lys
				260					265					270	Leu	
			275					280					285	His	Ala	
		290					295					300			Asn	
	Val	Ser	Ser	Ala	Thr	Pro	Lys	Gly	Gly	Ala	Ile	Ser	Ile	Asp	Ala	Ser

305					310					215					
	Glu	Leu	Ser	Leu		Ala	Glu	Thr	Gly	315	Tla	Th~	Dho	17- 1	320
•				325					330	N311	116	1111	PHE	335	Arg
Asn	Thr	Leu	Thr	Thr	Thr	Gly	Ser	Thr		Thr	Pro	Lvs	Ara	Asn	Ala
			340					345					350		
Ile	Asn	Ile	Gly	Ser	Asn	Gly	Lys	Phe	Thr	Glu	Leu	Arg	Ala	Ala	Lys
		355					360					365			
Asn	His	Thr	Ile	Phe	Phe	Tyr	Asp	Pro	Ile	Thr	Ser	Glu	Gly	Thr	Ser
Cox	370	17-1	T	T	- 1	375	_		_		380				
385	ASP	vai	Leu	гÀг	390	Asn	Asn	Gly	Ser		Gly	Ala	Leu	Asn	
	Gln	Glv	Thr	Tle		Phe	Ser	Glv	Glu	395 Th~	T 011	Th-	71-		400
•		1		405			001	Cry	410	1111	пеп	1111	Ald	415	GIU
Leu	Lys	Val	Ala	Asp	Asn	Leu	Lys	Ser		Phe	Thr	Gln	Pro	Val	Ser
			420					425					430		
Leu	Ser	Gly	Gly	Lys	Leu	Leu	Leu	Gln	Lys	Gly	Val	Thr	Leu	Glu	Ser
		435					440					445			
Thr	Ser 450	Phe	Ser	Gln	Glu	Ala	Gly	Ser	Leu	Leu		Met	Asp	Ser	Gly
Thr		Len	Ser	Thr	Th.~	455	C1	C =	т1 -	m\	460	 .	_	_	
465	****		Ser	1111	470	Ala	Gry	ser	ire	475	iie	Thr	Asn	Leu	
Ile	Asn	Val	Asp	Ser		Gly	Leu	Lvs	Gln		Val	Ser	Len	Thr	480
				485					490					495	
Lys	Gly	Ala	Ser	Asn	Lys	Val	Ile	Val	Ser	Gly	Lys	Leu	Asn	Leu	Ile
			500					505					510		
Asp	Ile	Glu	Gly	Asn	Ile	Tyr		Ser	His	Met	Phe		His	Asp	Gln
Len	Phe	515	T.Au	I au	Tvc	T l o	520	17-1			_	525	_		
200	530	361	Leu	ьец	цуз	535	1111	vaı	Asp	Ата	Asp 540	Val	Asp	Thr	Asn
Val		Ile	Ser	Ser	Leu		Pro	Val	Pro	Ala		Asn	Pro	Acn	Ser
545	_				550					555	O L u	тэр	110	non	560
Glu	Tyr	Gly	Phe	Gln	Gly	Gln	Trp	Asn	Val	Asn	Trp	Thr	Thr	Asp	Thr
				565					570					575	
Ala	Thr	Asn	Thr	Lys	Glu	Ala	Thr	Ala	Thr	Trp	Thr	Lys		Gly	Phe
Val	Pro	Ser	580 Pro		7 ~~	Lvc	S0=	585	T	11-1		_	590	_	_
		595	Pro	Gru	AL 9	nys	600	ALG	Leu	vai	Cys	605	Thr	Leu	Trp
Gly	Val		Thr	Asp	Ile	Arg		Leu	Gln	Gln	Leu	Val	Glu	Tle	Gly
	610					615					620				
Ala	Thr	Gly	Met	Glu	His	Lys	Gln	Gly	Phe	Trp	Val	Ser	Ser	Met	Thr
625					630					635					640
ASI	Pne	Leu	HIS	Lys 645	Thr	Gly	Asp	Glu	Asn	Arg	Lys	Gly	Phe		His
Thr	Ser	Glv	Glv		Val	Tla	Gly	C1	650	71-	*** -	m)-		655	_
		Cry	660	LYL	val	116	GLY	665	ser	Ala	HIS	Thr	670	Lys	Asp
Asp	Leu	Phe	Thr	Phe	Ala	Phe	Cys		Leu	Phe	Ala	Ara	Asp	I.vs	Asp
		675					680					685			
Cys	Phe	Ile	Ala	His	Asn	Asn	Ser	Arg	Thr	Tyr	Gly	Gly	Thr	Leu	Phe
	690					695					700				
705	гÀг	HIS	Ser	HIS	Thr	Leu	Gln	Pro	Gln		Tyr	Leu	Arg	Leu	Gly
	Ala	Lvc	Phe	Ser	710 Glu		Δ1	Tla	C3	715	nt-	D		~ 3	720 Ile
9		~,3	- 110	725	GIU	Ser	vrq	TIG	730	гÀЗ	rne	Pro	Arg		Ile
Pro	Leu	Ala	Leu		Val	Gln	Val	Ser		Ser	His	Ser	Acn	735 Asn	Arg
			740					745					750		
Met	Glu	Thr	His	Tyr	Thr	Ser	Leu	Pro	Glu	Ser	Glu	Gly	Ser	Trp	Ser
		755					760					765			



(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2815 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

		GTTAGTGCTC			TACTAGTTGT	60
		TGCTGAAAAT		CTGATAGCTT	TGACGGAAGT	120
		TCCTAAAAAT		GAATAGACTA	TACTCTGACA	180
GGAGATATAA	CTCTGCAAAA	CCTTGGGGAT	TCGGCAGCTT	TAACGAAGGG	TTGTTTTTCT	240
GACACTACGG	AATCTTTAAG	CTTTGCCGGT	AAGGGGTACT	CACTTTCTTT	TTTAAATATT	300
AAGTCTAGTG	CTGAAGGCGC	AGCACTTTCT	GTTACAACTG	ATAAAAATCT	GTCGCTAACA	360
GGATTTTCGA	GTCTTACTTT		CCATCATCGG			420
AAAGGTGCAG	TTAAATGTGG	AGGGGATCTT	ACATTTGATA	ACAATGGAAC	TATTTTATTT	480
AAACAAGATT	ACTGTGAGGA	AAATGGCGGA	GCCATTTCTA	CCAAGAATCT	TTCTTTGAAA	540
		TTTTGAAGGG				600
GGGGCTATTT	GTGCTACTGG					660
TCGAACAATA	TTGCTGAAGC	TGCAGGTGGA	GCTATAAATA	GCACAGGAAA	CTGTACAATT	720
ACAGGGAATA	CGTCTCTTGT	ATTTTCTGAA	AATAGTGTGA	CAGCGACCGC	AGGAAATGGA	780
GGAGCTCTTT		CGATGTTACC				840
GGAAACCAAG	CTGTAGCTAA	TGGCGGAGCC	ATTTATGCTA	AGAAGCTTAC	ACTGGCTTCC	900
GGGGGGGGG	GGGGTATCTC	CTTTTCTAAC	AATATAGTCC	AAGGTACCAC	TGCAGGTAAT	960
GGTGGAGCCA	TTTCTATACT	GGCAGCTGGA	GAGTGTAGTC	TTTCAGCAGA	AGCAGGGGAC	1020
ATTACCTTCA	ATGGGAATGC	CATTGTTGCA	ACTACACCAC	AAACTACAAA	AAGAAATTCT	1020
ATTGACATAG	GATCTACTGC	AAAGATCACG	AATTTACGTG		GCATAGCATC	1140
		TGCTAATACG			TTTAAATCTC	
		TAGTACAGAT				1200
				COMPTGITI	AADIDDIOLL	1260

AAGCTCTCTG	AAGATGAAGC	AAAAGTTGCA	GACAACCTCA	CTTCTACGCT	GAAGCAGCCT	1320
GTAACTCTAA	CTGCAGGAAA	TTTAGTACTT	AAACGTGGTG	TCACTCTCGA	TACGAAAGGC	1380
TTTACTCAGA	CCGCGGGTTC	CTCTGTTATT	ATGGATGCGG	GCACAACGTT	AAAAGCAAGT	1440
ACAGAGGAGG	TCACTTTAAC	AGGTCTTTCC	ATTCCTGTAG	ACTCTTTAGG	CGAGGGTAAG	1500
AAAGTTGTAA				CCCTTAGTGG	TCCGATTCTT	1560
CTTTTGGATA	ACCAAGGGAA	TGCTTATGAA	AATCACGACT	TAGGAAAAAC	TCAAGACTTT	1620
TCATTTGTGC	AGCTCTCTGC	TCTGGGTACT	GCAACAACTA	CAGATGTTCC	AGCGGTTCCT	1680
ACAGTAGCAA			CAAGGTACTT		TTGGGTTGAT	1740
GATACCGCAA	GCACTCCAAA	GACTAAGACA	GCGACATTAG	CTTGGACCAA	TACAGGCTAC	1800
CTTCCGAATC	CTGAGCGTCA	AGGACCTTTA	GTTCCTAATA	GCCTTTGGGG	ATCTTTTTCA	1860
GACATCCAAG	CGATTCAAGG	TGTCATAGAG	AGAAGTGCTT	TGACTCTTTG	TTCAGATCGA	1920
GGCTTCTGGG	CTGCGGGAGT	CGCCAATTTC	TTAGATAAAG	ATAAGAAAGG	GGAAAAACGC	1980
AAATACCGTC	ATAAATCTGG	TGGATATGCT	ATCGGAGGTG	CAGCGCAAAC	TTGTTCTGAA	2040
AACTTAATTA	GCTTTGCCTT	TTGCCAACTC	TTTGGTAGCG	ATAAAGATTT	CTTAGTCGCT	2100
AAAAATCATA	CTGATACCTA	TGCAGGAGCC	TTCTATATCC	AACACATTAC	AGAATGTAGT	2160
GGGTTCATAG	GTTGTCTCTT	AGATAAACTT	CCTGGCTCTT	GGAGTCATAA	ACCCCTCGTT	2220
TTAGAAGGGC	AGCTCGCTTA	TAGCCACGTC	AGTAATGATC	TGAAGACAAA	GTATACTGCG	2280
TATCCTGAGG	TGAAAGGTTC	TTGGGGGAAT	AATGCTTTTA	ACATGATGTT	GGGAGCTTCT	2340
TCTCATTCTT	ATCCTGAATA	CCTGCATTGT	TTTGATACCT	ATGCTCCATA	CATCAAACTG	2400
AATCTGACCT	ATATACGTCA	GGACAGCTTC	TCGGAGAAAG	GTACAGAAGG	AAGATCTTTT	2460
GATGACAGCA	ACCTCTTCAA	TTTATCTTTG	CCTATAGGGG	TGAAGTTTGA	GAAGTTCTCT	2520
GATTGTAATG	ACTITTCTTA	TGATCTGACT	TTATCCTATG	TTCCTGATCT	TATCCGCAAT	2580
GATCCCAAAT	GCACTACAGC	ACTTGTAATC	AGCGGAGCCT	CTTGGGAAAC	TTATGCCAAT	2640
AACTTAGCAC	GACAGGCCTT	GCAAGTGCGT	GCAGGCAGTC	ACTACGCCTT	CTCTCCTATG	2700
TTTGAAGTGC	TCGGCCAGTT		GTTCGTGGAT	CCTCACGGAT	TTATAATGTA	2760
GATCTTGGGG	GTAAGTTCCA	ATTCTAGGAG	CGTCTCTCAT	GTCTCAGAAA	TTCTG	2815

(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 928 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

			_					-							
1				5		Trp			10					15	_
Phe	Thr	Ser	Cys 20	Ser	Thr	Val	Phe	Ala 25	Ala	Thr	Ala	Glu	Asn 30	Ile	Gly
Pro	Ser	Asp 35	Ser	Phe	Asp	Gly	Ser 40	Thr	Asn	Thr	Gly	Thr 45	Tyr	Thr	Pro
Lys	Asn 50	Thr	Thr	Thr	Gly	Ile 55	Asp	Tyr	Thr	Leu	Thr 60	Gly	Asp	Ile	Thr
Leu 65	Gln	Asn	Leu	Gly	Asp 70	Ser	Ala	Ala	Leu	Thr 75	Lys	Gly	Cys	Phe	Ser 80
Asp	Thr	Thr	Glu	Ser 85	Leu	Ser	Phe	Ala	Gly 90	Lys	Gly	Tyr	Ser	Leu 95	
Phe	Leu	Asn	Ile 100	Lys	Ser	Ser	Ala	Glu 105	Gly	Ala	Ala	Leu	Ser 110	Val	Thr
Thr	Asp	Lys 115	Asn	Leu	Ser	Leu	Thr 120	Gly	Phe	Ser	Ser	Leu 125	Thr	Phe	Leu
Ala	Ala 130	Pro	Ser	Ser	Val	Ile 135	Thr	Thr	Pro	Ser	Gly 140	Lys	Gly	Ala	Val

_	_	_													
Lys 145	Cys	Gly	Gly	Asp	Leu 150	Thr	Phe	Asp	Asn	Asn 155	Gly	Thr	Ile	Leu	Phe 160
Lys	Gln	Asp	Tyr	Cys 165	Glu	Glu	Asn	Gly	Gly 170		Ile	Ser	Thr	Lys	Asn
Leu	Ser	Leu	Lys 180		Ser	Thr	Gly	Ser 185	Ile	Ser	Phe	Glu		175 Asn	Lys
Ser	Ser	Ala		Glv	Lvs	Lvs	Glv		Λla	Tlo	Cvra	71-	190	Gly	mı
		195		1	2,5	Lys	200	Gly	ALA	116	Cys	205	Inr	GIY	Thr
Val	Asp	Ile	Thr	Asn	Asn	Thr		Pro	Thr	T.eu	Dhe	205	λαπ	Asn	Tlo
	210					215			****	Deu	220	261	ASII	ASII	116
Ala	Glu	Ala	Ala	Gly	Gly		Ile	Asn	Ser	Thr	Glv	Asn	Cvs	Thr	Tle
225				. •	230					235	1	11011	Cys	1111	240
Thr	Gly	Asn	Thr	Ser	Leu	Val	Phe	Ser	Glu	Asn	Ser	Val	Thr	Ala	Thr
				245					250					255	
Ala	Gly	Asn	Gly	Gly	Ala	Leu	Ser	Gly	Asp	Ala	Asp	Val	Thr	Ile	Ser
			260					265					270		
Gly	Asn	Gln	Ser	Val	Thr	Phe	Ser	Gly	Asn	Gln	Ala	Val	Ala	Asn	Glv
		275					280					285			
Gly	Ala	Ile	Tyr	Ala	Lys	Lys	Leu	Thr	Leu	Ala	Ser	Gly	Gly	Gly	Gly
	290					295					300				
Gly	Ile	Ser	Phe	Ser	Asn	Asn	Ile	Val	Gln	Gly	Thr	Thr	Ala	Gly	Asn
305					310					315					320
GIY	Gly	Ala	Ile	Ser	Ile	Leu	Ala	Ala	Gly	Glu	Cys	Ser	Leu	Ser	Ala
61			_	325					330					335	
GIU	Ala	GIĀ	Asp	ile	Thr	Phe	Asn		Asn	Ala	Ile	Val	Ala	Thr	Thr
Dro	C1 ~		340	T	.	_	_	345		_			350		
PIO	GIII	355	Inr	гÀг	Arg	Asn	Ser	Ile	Asp	Ile	Gly		Thr	Ala	Lys
Tle	Thr		T Au	7~~	7 1 -	T1 -	360	G 1		_		365			
110	370	ASII	neu	Arg	Ald	375	ser	GTÅ	HIS	Ser		Phe	Phe	Tyr	Asp
Pro		Thr	Δla	Δen	Thr		ר ו ת	7.00	Com	Th	380	en)	_		_
385			,,,,u	non	390	Ata	Ala	ASP	ser		Asp	Thr	Leu	Asn	
	Lvs	Ala	Asp	Ala		Asn	Ser	Thr	λcn	395	C	C1	C	Ile	400
			<u>F</u>	405	017		JCI	1111	410	ıyı	ser	GIY	ser		vai
Phe	Ser	Gly	Glu		Leu	Ser	Glu	Asp	Glu	·Δla	Lve	V = 1	λ1 =	415 Asp	Nan
		•	420	•				425	010		Lys	٧	430	Asp	ASII
Leu	Thr	Ser	Thr	Leu	Lys	Gln	Pro		Thr	Leu	Thr	Ala	Glv	Asn	Len
	I	435					440					445			
Val	Leu	Lys	Arg	Gly	Val	Thr	Leu	Asp	Thr	Lys	Gly	Phe	Thr	Gln	Thr
	450		-			455					460				
Ala	Gly	Ser	Ser	Val	Ile	Met	Asp	Ala	Gly	Thr	Thr	Leu	Lys	Ala	Ser
465					470					475					480
Thr	Glu	Glu	Val	Thr	Leu	Thr	Gly	Leu	Ser	Ile	Pro	Val	Asp	Ser	Leu
				485					490					495	
GLY	GLu	GLY	Lys	Lys	Val	Val	Ile	Ala	Ala	Ser	Ala	Ala	Ser	Lys	Asn
17-1	71-	.	500		_		_	505					510		
val	Ата	Leu	Ser	GLY	Pro	Ile	Leu	Leu	Leu	Asp	Asn	Gln	Gly	Asn	Ala
Trees	<i>α</i> 1	515		*		~ 1	520					525			
IAT	GIU	. ASN	HIS	Asp	Leu	GLY	Lys	Thr	Gln	Asp		Ser	Phe	Val	Gln
[.au	530		T ou	C1.	. The	535				_	540				
545	Jel	MIG	neu	. сту			Inr	Thr	Thr			Pro	Ala	Val	Pro
		Δla	Th~	D~~	550 Thr		т		. m	555	C 3		-		560
				565		1112	TAL	GTĀ			GTĀ	Thr	Trp		Met
Thr	Tro	Val	Asn			Δla	Ser	Th~	570	Luc	Th	T	m).	575	Thr
· -			580		- ***			585		пλя	IIII	ьys			Thr
Leu	Ala	Tro			Thr	Glv	Tvr			Acn	Pro	G1 11	590	C1 -	Gly
		-				1						-14		CTIT	GIY

		595					600					605			
Pro	Leu 610	Val	Pro	Asn	Ser	Leu 615	Trp	Gly	Ser	Phe	Ser 620	Asp	Ile	Gln	Ala
625		Gly			630					635	Leu				640
Gly	Phe	Trp	Ala	Ala 645	Gly	Val	Ala	Asn	Phe 650	Leu	Asp	Lys	Asp	Lys 655	Lys
		Lys	660					665					670		
		Ala 675		-			680					685			
	690	Phe				695					700				
705		Tyr			710					715					720
		Ile		725					730					735	
		Leu	740					745					750		
		Lys 755					760					765			
	770	Asn				775					780				_
785		Tyr			790					795					800
		Thr		805					810					815	
		Ser	820					825					830		
		Lys 835					840					845			
	850	Leu				855					860				
865		Ala			870					875					880
		Ala		885					890					895	
		Pro	500					905					910		
Gly	Ser	Ser 915	Arg	Ile	Tyr	Asn	Val 920		Leu	Gly	Gly	Lys		Gln	Phe

(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3052 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ATGCGATTTT	CGCTCTGCGG	ATTTCCTCTA	GTTTTTTCTT	TAACATTGCT	CTCAGTCTTC	60
					TCATGGAGAT	120
					CCTTACTGGT	180

a						
GATGTCTCAA	TATCTAACGT	CGATAACTCT	GCATTAAATA	AAGCCTGCTT	CAATGTGACC	240
TCAGGAAGTG	TGACGTTCGC	AGGAAATCAT	CATGGGTTAT	ATTTTAATAA	TATTTCCTCA	300
GGAACTACAA	AGGAAGGGC	TGTACTTTGT	TGCCAAGATC	CTCAAGCAAC	GGCACGTTTT	360
TCTGGGTTCT	CCACGCTCTC	TTTTATTCAG	AGCCCCGGAG	ATATTAAAGA	ACAGGGATGT	420
CTCTATTCAA	AAAATGCACT	TATGCTCTTA	AACAATTATG	TAGTGCGTTT	TGAACAAAAC	480
CAAAGTAAGA	CTAAAGGCGG	AGCTATTAGT	GGGGCGAATG	TTACTATAGT	AGGCAACTAC	540
GATTCCGTCT	CTTTCTATCA	GAATGCAGCC	ACTTTTGGAG	GTGCTATCCA	TTCTTCAGGT	600
CCCCTACAGA	TTGCAGTAAA	TCAGGCAGAG	ATAAGATTTG	CACAAAATAC	TGCCAAGAAT	660
GGTTCTGGAG	GGGCTTTGTA	CTCCGATGGT	GATATTGATA	TTGATCAGAA	TGCTTATGTT	720
CTATTTCGAG	AAAATGAGGC	ATTGACTACT	GCTATAGGTA	AGGGAGGGC	ТСТСТСТТСТ	780
CTTCCCACTT	CAGGAAGTAG	TACTCCAGTT	CCTATTGTGA	CTTTCTCTGA	CAATAAACAG	840
TTAGTCTTTG	AAAGAAACCA	TTCCATAATG	GGTGGCGGAG	CCATTTATGC	TAGGAAACTT	900
AGCATCTCTT	CAGGAGGTCC	TACTCTATTT	ATCAATAATA	TATCATATGC	AAATTCGCAA	960
AATTTAGGTG	GAGCTATTGC	CATTGATACT	GGAGGGGAGA	TCAGTTTATC	AGCAGAGAAA	1020
GGAACAATTA	CATTCCAAGG	AAACCGGACG	AGCTTACCGT	TTTTGAATGG	CATCCATCTT	1080
TTACAAAATG	CTAAATTCCT	GAAATTACAG	GCGAGAAATG	GATGCTCTAT	AGAATTTAT	1140
GATCCTATTA	CTTCTGAAGC	AGATGGGTCT	ACCCAATTGA	ATATCAACGG	AGATCCTAAA	1200
AATAAAGAGT	ACACAGGGAC	CATACTCTTT	TCTGGAGAAA	AGAGTCTAGC	AAACGATCCT	1260
AGGGATTTTA	AATCTACAAT	CCCTCAGAAC	GTCAACCTGT	CTGCAGGATA	CTTAGTTATT	1320
AAAGAGGGGG	CCGAAGTCAC	AGTTTCAAAA	TTCACGCAGT	CTCCAGGATC	GCATTTACTT	1380
TTAGATTTAG	GAACCAAACT	GATAGCCTCT	AAGGAAGACA	TTGCCATCAC	AGGCCTCGCC	1440
ATAGATATAG	ATAGCTTAAG	CTCATCCTCA	ACAGCAGCTG	TTATTAAAGC	AAACACCCCA	1500
AATAAACAGA	TATCCGTGAC	GGACTCTATA	GAACTTATCT	CGCCTACTGG	CAATGCCTAT	1560
GAAGATCTCA	GAATGAGAAA	TTCACAGACG	TTCCCTCTGC	TCTCTTTAGA	GCCTGGAGCC	1620
GGGGGTAGTG	TGACTGTAAC	TGCTGGAGAT	TTCCTACCGG	TAAGTCCCCA	TTATCCTTTT	1680
CAAGGCAATT	GGAAATTAGC	TTGGACAGGA	ACTGGAAACA	AAGTTGGAGA	ATTCTTCTCC	1740
GATAAAATAA	ATTATAAGCC	TAGACCTGAA	AAAGAAGGAA	ATTTACTTCC	TAATATCTTC	1800
TGGGGGAATG	CTGTAAATGT	CAGATCCTTA	ATGCAGGTTC	AAGAGACCCA	TGCATCGAGC	1860
TTACAGACAG	ATCGAGGGCT	GTGGATCGAT	GGAATTGGGA	ATTTCTTCCA	TGTATCTGCC	1920
TCCGAAGACA	ATATAAGGTA	CCGTCATAAC	AGCGGTGGAT	ATGTTCTATC	TGTAAATAAT	
GAGATCACAC	CTAAGCACTA	TACTTCGATG	GCATTTTCCC	AACTCTTTAG	TAGAGACAAG	1980 2040
GACTATGCGG	TTTCCAACAA	CGAATACAGA	ATGTATTTAG	GATCGTATCT	CTATCAATAT	2100
ACAACCTCCC	TAGGGAATAT	TTTCCGTTAT	GCTTCGCGTA	ACCCTAATGT	AAACGTCGGG	2160
ATTCTCTCAA	GAAGGTTTCT	TCAAAATCCT	CTTATGATTT	TTCATTTTCT	GTGTGCTTAT	2220
GGTCATGCCA	CCAATGATAT	GAAAACAGAC	TACGCAAATT	TCCCTATGGT	GAAAAACAGC	2220
TGGAGAAACA	ATTGTTGGGC	TATAGAGTGC	GGAGGGAGCA	TGCCTCTATT	GGTATTTGAG	2340
AACGGAAGAC	TTTTCCAAGG	TGCCATCCCA	TTTATGAAAC	TACAATTAGT	TTATCCTTAT	2400
CAGGGAGATT	TCAAAGAGAC	GACTGCAGAT	GGCCGTAGAT	TTAGTAATGG	GAGTTTAACA	2460
TCGATTTCTG	TACCTCTAGG	CATACGCTTT	GAGAAGCTGG	CACTTTCTCA	GGATGTACTC	2520
TATGACTTTA	GTTTCTCCTA	TATTCCTGAT	ATTTTCCGTA	AGGATCCCTC	ATCTCAACCT	
GCTCTGGTGA	TTAGCGGAGA	CTCCTGGCTT	GTTCCGGCAG	CACACGTATC	AAGACATGCT	2580 2640
TTTGTAGGGA	GTGGAACGGG	TCGGTATCAC	TTTAACGACT	ATACTGAGCT	CTTATCTCCA	
GGAAGTATAG	AATGCCGCCC	CCATGCTAGG	AATTATAATA	TAAACTGTGG	A A C C A A A TO TOTAL	2700
CGTTTTTAGA	AGGTTTCCAT	TGCCTGTGTG	GTTCCGGATC	TTAACTATAA	ATCCTCCACT	2760
ATGGATCATA	GGCATTGGGT	TTCTCGAACT	TGTGTGGAGA	ATAACGACAT	TTTATATATA	2820
TAACGGAATA	CTCGTATCAC	CTCAGCCCCT	AGAGACATTC	TTTAGGGGGTT	TIAIAIGCA	2880
CTAAACTTCG	TATTTTATCG	AGAATCCTTT	ACGTTCTTGG	TTTGCTTGTC	TCCGAGGACT	2940
TCTCTAACGA	ATCATAGGGA	TTCCAGGGTT	CTGTTCCTTC	AGTCCTTTCC	CA	3000
				01/4/11/00	CA	3052

(2) INFORMATION FOR SEQ ID NO:6:

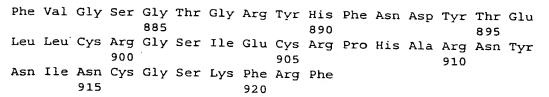
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 922 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

1				5					10			Ser		1 =	
Leu	Ser	Val	Phe 20	Asp	Thr	Ser	Leu	Ser 25	Ala	Thr	Thr	Ile		Leu	Thr
Pro	Glu	Asp 35	Ser	Phe	His	Gly	Asp 40	Ser	Gln	Asn	Ala	Glu	30 Arg	Ser	Tyr
Asn	Val 50	Gln	Ala	Gly	Asp	Val 55		Ser	Leu	Thr		45 Asp	Val	Ser	Ile
Ser 65	Asn	Val	Asp	Asn	Ser 70		Leu	Asn	Lys	Ala 75	60 Cys	Phe	Asn	Val	
Ser	Gly	Ser	Val	Thr 85		Ala	Gly	Asn	His 90	His	Gly	Leu	Tyr		80 Asn
Asn	Ile	Ser	Ser 100		Thr	Thr	Lys	Glu 105	Gly	Ala	Val	Leu		95 Cys	Gln
Asp	Pro	Gln 115		Thr	Ala	Arg	Phe 120	Ser	Gly	Phe	Ser	Thr	110 Leu	Ser	Phe
Ile	Gln 130		Pro	Gly	Asp	Ile 135		Glu	Gln	Gly		125 Leu	Tyr	Ser	Lys
Asn 145		Leu	Met	Leu	Leu 150		Asn	Tyr	Val	Val 155	140 Arg	Phe	Glu	Gln	
Gln	Ser	Lys	Thr	Lys 165		Gly	Ala	Ile	Ser 170	Gly	Ala	Asn	Val		160 Ile
Val	Gly	Asn	Tyr 180		Ser	Val	Ser	Phe 185	Tyr	Gln	Asn	Ala		175 Thr	Phe
Gly	Gly	Ala 195		His	Ser	Ser	Gly 200	Pro	Leu	Gln	Ile	Ala	190 Val	Asn	Gln
Ala	Glu 210	Ile	Arg	Phe	Ala	Gln 215	Asn	Thr	Ala	Lys	Asn 220	205 Gly	Ser	Gly	Gly
Ala 225	Leu	Tyr	Ser	Asp	Gly 230		Ile	Asp	Ile		Gln	Asn	Ala	Tyr	
Leu	Phe	Arg	Glu	Asn 245		Ala	Leu	Thr	Thr 250	235 Ala	Ile	Gly	Lys		240 Gly
Ala	Val	Cys	Cys 260		Pro	Thr	Ser	Gly 265	Ser	Ser	Thr	Pro		255 Pro	Ile
Val	Thr	Phe 275		Asp	Asn	Lys	Gln 280	Leu	Val	Phe	Glu	Arg	270 Asn	His	Ser
Ile	Met 290	Gly	Gly	Gly	Ala	Ile 295	Tyr	Ala	Arg	Lys		285 Ser	Ile	Ser	Ser
Gly 305	Gly	Pro	Thr	Leu	Phe 310		Asn	Asn	Ile	Ser 315	300 Tyr	Ala	Asn	Ser	
Asn	Leu	Gly	Gly	Ala 325		Ala	Ile	Asp	Thr	Gly	Gly	Glu	Ile		320 Leu
Ser	Ala	Glu	Lys 340		Thr	Ile	Thr	Phe	Gln	Gly	Asn	Arg		335 Ser	Leu
Pro	Phe	Leu 355	Asn	Gly	Ile	His	Leu 360	Leu	Gln	Asn	Ala	Lys	350 Phe	Leu	Lys
Leu	Gln 370		Arg	Asn	Gly	Cys 375		Ile	Glu	Phe	Tyr 380	365 Asp	Pro	Ile	Thr
Ser 385	Glu	Ala	Asp	Gly	Ser 390		Gln	Leu	Asn		Asn	Gly	Asp	Pro	
	Lys	Glu	Tyr	Thr 405		Thr	Ile	Leu	Phe	395 Ser	Gly	Glu	Lys		400 Leu
Ala	Asn	Asp	Pro		Asp	Phe	Lys	Ser	Thr	Ile	Pro	Gln	Asn	415 Val	Asn

			420												
Leu	Ser	Δla		Tur	Lau	V-3	т1 -	425	G1	0. 1			430		
200		435	Ory	T Y L	Leu	Vai	440	Lys	GIU	GIĀ	Ala		Val	Thr	Val
Ser	Lys 450		Thr	Gln	Ser	Pro		Ser	His	Leu	Val 460	445 Leu	Asp	Leu	Gly
Thr 465	Lys	Leu	Ile	Ala	Ser 470		Glu	Asp	Ile	Ala 475	Ile	Thr	Gly	Leu	
Ile	Asp	Ile	Asp	Ser	Leu	Ser	Ser	Ser	Ser 490	Thr	Ala	Ala	Val		480 Lys
Ala	Asn	Thr	Ala 500		Lys	Gln	Ile	Ser 505	Val	Thr	Asp	Ser		495 Glu	Leu
Ile	Ser	Pro 515	Thr	Gly	Asn	Ala	Tyr 520		Asp	Leu	Arg	Met 525	510 Arg	Asn	Ser
Gln	Thr 530	Phe	Pro	Leu	Leu	Ser 535		Glu	Pro	Gly	Ala 540	Gly	Gly	Ser	Val
545					Asp 550					555	Pro				560
				565	Leu				570	Thr				575	Gly
			580		Lys			585					590	Lys	
		595			Asn		600					605			
	PIO				Gln	615					620				
625					Asp 630					635					640
				645	Arg				650					655	
			990		Ile			665					670		
		6/5			Arg		680					685			
	690			-	Gly	695					700				
/05					Tyr 710					715					720
				725	Phe His				730					725	
			740		Lys			745					750		
		155			Met		760					765			
	//0				Pro	775					780				
/85					790 Glu					795					800
				805	Ile				810					815	
			820		Asp			825					830		
		835			Lys		840					845			
	820				Leu	855					860				
865	•	•			870				•110	875	val	ser	ar.g	nis	880



(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2526 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

ATGAAGATTC	CACTCCGCTT	TTTATTGATA	TCATTAGTAC	CTACGCTTTC	TATGTCGAAT	60
TTATTAGGAG	CTGCTACTAC	CGAAGAGCTA	TCGGCTAGCA	ATAGCTTCGA	TGGAACTACA	120
TCAACAACAA	GCTTTTCTAG	TAAAACATCA	TCGGCTACAG	ATGGCACCAA	TTATGTTTTT	180
AAAGATTCTG	TAGTTATAGA	AAATGTACCC	AAAACAGGGG	AAACTCAGTC	TACTAGTTGT	240
TTTAAAAATG	ACGCTGCAGC	TGGAGATCTA	AATTTCTTAG	GAGGGGGATT	TTCTTTCACA	300
TTTAGCAATA	TCGATGCAAC	CACGGCTTCT	GGAGCTGCTA	TTGGAAGTGA	AGCAGCTAAT	360
AAGACAGTCA	CGTTATCAGG	ATTTTCGGCA	CTTTCTTTTC	TTAAATCCCC	AGCAAGTACA	420
GTGACTAATG	GATTGGGAGC	TATCAATGTT	AAAGGGAATT	TAAGCCTATT	GGATAATGAT	480
AAGGTATTGA	TTCAGGACAA	TTTCTCAACA	GGAGATGGCG	GAGCAATTAA	TTGTGCAGGC	540
TCCTTGAAGA	TCGCAAACAA	TAAGTCCCTT	TCTTTTATTG	GAAATAGTTC	TTCAACACGT	600
GGCGGAGCGA	TTCATACCAA	AAACCTCACA	CTATCTTCTG	GTGGGGAAAC	TCTATTTCAG	660
GGGAATACAG	CGCCTACGGC	TGCTGGTAAA	GGAGGTGCTA	TCGCGATTGC	AGACTCTGGC	720
ACCCTATCCA	TTTCTGGAGA	CAGTGGCGAC	ATTATCTTTG	AAGGCAATAC	GATAGGAGCT	780
ACAGGAACCG	TCTCTCATAG	TGCTATTGAT	TTAGGAACTA	GCGCTAAGAT	AACTGCGTTA	840
CGTGCTGCGC	AAGGACATAC	GATATACTTT	TATGATCĊGA	TTACTGTAAC	AGGATCGACA	900
TCTGTTGCTG	ATGCTCTCAA	TATTAATAGC	CCTGATACTG	GAGATAACAA	AGAGTATACG	960
GGAACCATAG	TCTTTTCTGG	AGAGAAGCTC	ACGGAGGCAG	AAGCTAAAGA	TGAGAAGAAC	1020
CGCACTTCTA	AATTACTTCA	AAATGTTGCT	TTTAAAAATG	GGACTGTAGT	TTTAAAAGGT	1080
GATGTCGTTT	TAAGTGCGAA	CGGTTTCTCT	CAGGATGCAA	ACTCTAAGTT	GATTATGGAT	1140
TTAGGGACGT	CGTTGGTTGC	AAACACCGAA	AGTATCGAGT	TAACGAATTT	GGAAATTAAT	1200
ATAGACTCTC	TCAGGAACGG	GAAAAAGATA	AAACTCAGTG	CTGCCACAGC	TCAGAAAGAT	1260
ATTCGTATAG	ATCGTCCTGT	TGTACTGGCA	ATTAGCGATG	AGAGTTTTTA	TCAAAATGGC	1320
TTTTTGAATG	AGGACCATTC	CTATGATGGG	ATTCTTGAGT	TAGATGCTGG	GAAAGACATC	1380
GTGATTTCTG	CAGATTCTCG	CAGTATAAAT	GCTGTACAAT	CTCCGTATGG	CTATCAGGGA	1440
AAGTGGACAA	TCAATTGGTC	TACTGATGAT	AAGAAAGCTA	CGGTTTCTTG	GGCAAAGCAA	1500
AGTTTTAATC	CCACTGCTGA	GCAGGAGGCT	CCGTTAGTTC	CTAATCTTCT	TTGGGGTTCT	1560
TTTATAGATG	TTCGTCCCTT	CCAAAATTTT	ATAGAGCTAG	GTACTGAAGG	TGCTCCTTAC	1620
GAAAAGAGAT	TTTGGGTTGC	AGGCATTTCC	AATGTTTTGC	ATAGGAGCGG	TCGTGAAAAT	1680
CAAAGGAAAT	TCCGTCATGT	GAGTGGAGGT	GCTGTAGTAG	GTGCTAGCAC	GAGGATGCCG	1740
GGTGGTGATA	CCTTGTCTCT	GGGTTTTGCT	CAGCTCTTTG	CGCGTGACAA	AGACTACTT	1800
ATGAATACCA	ATTTCGCAAA	GACCTACGCA	GGATCTTTAC	GTTTGCAGCA	CGATGCTTCC	1860
CTATACTCTG	TGGTGAGTAT	CCTTTTAGGA	GAGGGAGGAC	TCCGCGAGAT	CCTGTTGCCT	1920
TATGTTTCCA	AGACTCTGCC	GTGCTCTTTC	TATGGGCAGC	TTAGCTACGG	CCATACGGAT	1980
CATCGCATGA	AGACCGAGTC	TCTACCCCCC	CCCCCCCGA	CGCTCTCGAC	GGATCATACT	2040
TCTTGGGGAG	GATATGTCTG	GGCTGGAGAG	CTGGGAACTC	GAGTTGCTGT	TGAAAATACC	2100
AGCGGCAGAG	GATTTTTCCG	AGAGTACACT	CCATTTGTAA	AAGTCCAAGC	TGTTTACTCG	2160
CGCCAAGATA	GCTTTGTTGA	ACTAGGAGCT	ATCAGTCGTG	ATTTTAGTGA	TTCGCATCTT	2220
TATAACCTTG	CGATTCCTCT	TGGAATCAAG	TTAGAGAAAC	GGTTTGCAGA	GCAATATTAT	2280

CATGTTGTAG CGATGTATTC	TCCAGATGTT	TGTCGTAGTA	ACCCCAAATG	TACGACTACC	2340
CTACTTTCCA ACCAAGGGAG	TTGGAAGACC	AAAGGTTCGA	ACTTAGCAAG	ACAGGCTGGT	2400
ATTGTTCAGG CCTCAGGTTT	TCGATCTTTG	GGAGCTGCAG	CAGAGCTTTT	CGGGAACTTT	2460
GGCTTTGAAT GGCGGGGATC	TTCTCGTAGC	TATAATGTAG	ATGCGGGTAG	CAAAATCAAA	2520
TTTTAG					2526
					2526

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 841 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

N		~ 1	_		_										
1	Lys			5					10					15	
	Met		20					25					30		
Ser	Asn	Ser 35	Phe	Asp	Gly	Thr	Thr 40	Ser	Thr	Thr	Ser	Phe 45	Ser	Ser	Lys
Thr	Ser 50	Ser	Ala	Thr	Asp	Gly 55	Thr	Asn	Tyr	Val	Phe	Lys	Asp	Ser	Val
Val 65	Ile	Glu	Asn	Val	Pro 70	Lys	Thr	Gly	Glu	Thr 75	Gln	Ser	Thr	Ser	Cys 80
Phe	Lys	Asn	Asp	Ala 85	Ala	Ala	Gly	Asp	Leu 90		Phe	Leu	Gly	Gly 95	Gly
Phe	Ser	Phe	Thr 100	Phe	Ser	Asn	Ile	Asp		Thr	Thr	Ala	Ser 110	Gly	Ala
Ala	Ile	Gly 115	Ser	Glu	Ala	Ala	Asn 120		Thr	Val	Thr	Leu 125	Ser	Gly	Phe
Ser	Ala 130	Leu	Ser	Phe	Leu	Lys 135		Pro	Ala	Ser	Thr	Val	Thr	Asn	Gly
Leu 145	Gly	Ala	Ile	Asn	Val 150		Gly	Asn	Leu	Ser 155	Leu	Leu	Asp	Asn	
Lys	Val	Leu	Ile	Gln 165		Asn	Phe	Ser	Thr 170	Gly	Asp	Gly	Gly		160 Ile
Asn	Cys	Ala	Gly 180		Leu	Lys	Ile	Ala 185		Asn	Lys	Ser		175 Ser	Phe
Ile	Gly	Asn 195		Ser	Ser	Thr	Arg 200		Gly	Ala	Ile		190 Thr	Lys	Asn
Leu	Thr 210	Leu	Ser	Ser	Gly	Gly 215		Thr	Leu	Phe	Gln 220	205 Gly	Asn	Thr	Ala
Pro 225	Thr	Ala	Ala	Gly	Lys 230		Gly	Ala	Ile	Ala 235	Ile	Ala	Asp	Ser	
Thr	Leu	Ser	Ile	Ser 245		Asp	Ser	Gly	Asp 250	Ile	Ile	Phe	Glu		240 Asn
Thr	Ile	Gly	Ala 260		Gly	Thr	Val	Ser 265	His	Ser	Ala	Ile		255 Leu	Gly
Thr	Ser	Ala 275		Ile	Thr	Ala	Leu 280	Arg	Ala	Ala	Gln		270 His	Thr	Ile
Tyr	Phe 290		Asp	Pro	Ile	Thr 295		Thr	Gly	Ser		285 Ser	Val	Ala	Asp
Ala	Leu	Asn	Ile	Asn	Ser		Asp	Thr	Gly	Asp	300 Asn	Lys	Glu	Tyr	Thr

305					310					315					320
				325					330	Thr				Ala 335	Lys
			340					345					350	Phe	_
		355					360					365		Asn	_
	370					375					380			Thr	
385				-	390					395				Ile	400
				405					410					Ala 415	
			420					425					430	Ile	
		435					440					445		Ser	_
	450					455					460			Ser	
465					470					475				Gln	480
				485					490					Val 495	
			500					505					510	Pro	
		515					520					525		Phe	
	530					535					540			Arg	
545					550					555				Glu	560
				565					570					Ala 575	
			580					585					590	Gln	
		595					600					605		Lys	
	610					615					620			Ser	
625					630					635				Leu	640
				645					650					Ser 655	
			660					665					670	Pro	
		675					680					685		Trp	
	690					695					700			Arg	
705					710					715				Tyr	720
				725					730					Phe 735	
			740					745					750	Leu	
пÀг	Arg	755		Glu	Gln	Tyr	Tyr 760		Val	Val	Ala	Met 765		Ser	Pro

(2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2787 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATGAAGTCTT	CTTTCCCCAA	GTTTGTATTT	TCTACATTTG	CTATTTTCCC	TTTGTCTATG	60
ATTGCTACCG	AGACAGTTTT	GGATTCAAGT	GCGAGTTTCG	ATGGGAATAA	AAATGGTAAT	120
TTTTCAGTTC	GTGAGAGTCA	GGAAGATGCT	GGAACTACCT	ACCTATTTAA	GGGAAATGTC	180
ACTCTAGAAA	ATATTCCTGG	AACAGGCACA	GCAATCACAA	AAAGCTGTTT	TAACAACACT	240
AAGGGCGATT	TGACTTTCAC	AGGTAACGGG	AACTCTCTAT	TGTTCCAAAC	GGTGGATGCA	300
GGGACTGTAG	CAGGGGCTGC	TGTTAACAGC	AGCGTGGTAG	ATAAATCTAC	CACGTTTATA	360
GGGTTTTCTT	CGCTATCTTT	TATTGCGTCT	CCTGGAAGTT	CGATAACTAC	CGGCAAAGGA	420
GCCGTTAGCT	GCTCTACGGG	TAGCTTGAAG	TTTGACAAAA	ATGTCAGTTT	GCTCTTCAGC	480
AAAAACTTTT	CAACGGATAA	TGGCGGTGCT	ATCACCGCAA	AAACTCTTTC	ATTAACAGGG	540
ACTACAATGT	CAGCTCTGTT	TTCTGAAAAT	ACCTCCTCAA	AGAAAGGCGG	AGCCATTCAG	600
ACTTCCGATG	CCCTTACCAT	TACTGGAAAC	CAAGGGGAAG	TCTCTTTTTC	TGACAATACT	660
TCTTCGGATT	CTGGAGCTGC	AATTTTTACA	GAAGCCTCGG	TGACTATTTC	TAATAATGCT	720
AAAGTTTCCT	TTATTGACAA	TAAGGTCACA	GGAGCGAGCT	CCTCAACAAC	GGGGGATATG	780
TCAGGAGGTG	CTATCTGTGC	TTATAAAACT	AGTACAGATA	CTAAGGTCAC	CCTCACTGGA	840
AATCAGATGT	TACTCTTCAG	CAACAATACA	TCGACAACAG	CGGGAGGAGC	TATCTATGTG	900
AAAAAGCTCG	AACTGGCTTC	CGGAGGACTT	ACCCTATTCA	GTAGAAATAG	TGTCAATGGA	960
GGTACAGCTC	CTAAAGGTGG	AGCCATAGCT	ATCGAAGATA	GTGGGGAATT	GAGTTTATCC	1020
GCCGATAGTG	GTGACATTGT	CTTTTTAGGG	AATACAGTCA	CTTCTACTAC	TCCTGGGACG	1080
AATAGAAGTA	GTATCGACTT	AGGAACGAGT	GCAAAGATGA	CAGCTTTGCG	TTCTGCTGCT	1140
GGTAGAGCCA	TCTACTTCTA	TGATCCCATA	ACTACAGGAT	CTTCCACAAC	AGTTACAGAT	1200
GTCTTAAAAG	TTAATGAGAC	TCCGGCAGAT	TCTGCACTAC	AATATACAGG	GAACATCATC	1260
TTCACAGGAG	AAAAGTTATC	AGAGACAGAG	GCCGCAGATT	CTAAAAATCT	TACTTCGAAG	1320
CTACTACAGC	CTGTAACTCT	TTCAGGAGGT	ACTCTATCTT	TAAAACATGG	AGTGACTCTG	1380
CAGACTCAGG	CATTCACTCA	ACAGGCAGAT	TCTCGTCTCG	AAATGGACGT	AGGAACTACT	1440
CTAGAACCTG	CTGATACTAG	CACCATAAAC	AATTTGGTCA	TTAACATCAG	TTCTATAGAC	1500
GGTGCAAAGA	AGGCAAAAAT	AGAAACCAAA	GCTACGTCAA	AAAATCTGAC	TTTATCTGGA	1560
ACCATCACTT	TATTGGACCC	GACGGGCACG	TTTTATGAAA	ATCATAGTTT	AAGAAATCCT	1620
CAGTCCTACG	ACATCTTAGA	GCTCAAAGCT	TCTGGAACTG	TAACAAGCAC	CGCAGTGACT	1680
CCAGATCCTA	TAATGGGTGA	GAAATTCCAT	TACGGCTATC	AGGGAACTTG	GGGCCCAATT	1740
GTTTGGGGGA	CAGGGGCTTC	TACGACTGCA	ACCTTCAACT	GGACTAAAAC	TGGCTATATT	1800
CCTAATCCCG	AGCGTATCGG	CTCTTTAGTC	CCTAATAGCT	TATGGAATGC	ATTTATAGAT	1860
ATTAGCTCTC	TCCATTATCT	TATGGAGACT	GCAAACGAAG	GGTTGCAGGG	AGACCGTGCT	1920
TTTTGGTGTG	CTGGATTATC	TAACTTCTTC	CATAAGGATA	GTACAAAAAC	ACGACGCGGG	1980
TTTCGCCATT	TGAGTGGCGG	TTATGTCATA	GGAGGAAACC	TACATACTTG	TTCAGATAAG	2040

ATTCTTAGTG	CTGCATTTTG	TCAGCTCTTT	GGAAGAGATA	GAGACTACTT	TGTAGCTAAG	2100
AATCAAGGTA	CAGTCTACGG	AGGAACTCTC	TATTACCAGC	ACAACGAAAC	CTATATCTCT	2160
CTTCCTTGCA	AACTACGGCC	TTGTTCGTTG	TCTTATGTTC	CTACAGAGAT	TCCTGTTCTC	2220
TTTTCAGGAA	ACCTTAGCTA	CACCCATACG	GATAACGATC	TGAAAACCAA	GTATACAACA	2280
TATCCTACTG	TTAAAGGAAG	CTGGGGGAAT	GATAGTTTCG	CTTTAGAATT	CGGTGGAAGA	2340
GCTCCGATTT	GCTTAGATGA	AAGTGCTCTA	TTTGAGCAGT	ACATGCCCTT	CATGAAATTG	2400
CAGTTTGTCT	ATGCACATCA	GGAAGGTTTT	AAAGAACAGG	GAACAGAAGC	TCGTGAATTT	2460
GGAAGTAGCC	GTCTTGTGAA	TCTTGCCTTA	CCTATCGGGA	TCCGATTTGA	TAAGGAATCA	2520
GACTGCCAAG	ATGCAACGTA	CAATCTAACT	CTTGGTTATA	CTGTGGATCT	TGTTCGTAGT	2580
AACCCCGACT	GTACGACAAC	ACTGCGAATT	AGCGGTGATT	CTTGGAAAAC	CTTCGGTACG	2640
AATTTGGCAA	GACAAGCTTT	AGTCCTTCGT	GCAGGGAACC	ATTTTTGCTT	TAACTCAAAT	2700
TTTGAAGCCT	TTAGCCAATT	TTCTTTTGAA	TTGCGTGGGT	CATCTCGCAA	TTACAATGTA	2760
	CAAAATACCA					2787

(2) INFORMATION FOR SEQ ID NO:10:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 928 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

1				5					10					Ile 15	
			20					25					30	Ala	
		35					40					45		Gln	
	50					55					60			Glu	
65					70					75				Asn	80
	ž.			85					90					Phe 95	
			100					105					110	Ser	
		115					120					125	Ser	Phe	
	130					135					140			Ser	
Ser 145	Thr	Gly	Ser	Leu	Lys 150	Phe	Asp	Lys	Asn	Val 155	Ser	Leu	Leu	Phe	Ser 160
				165					170					Thr 175	Leu
Ser	Leu	Thr	Gly 180	Thr	Thr	Met	Ser	Ala 185	Leu	Phe	Ser	Glu	Asn 190	Thr	Ser
		195					200					205	Thr	Ile	
Gly	Asn 210	Gln	Gly	Glu	Val	Ser 215	Phe	Ser	Asp	Asn	Thr 220	Ser	Ser	Asp	Ser
Gly 225	Ala	Ala	Ile	Phe	Thr 230	Glu	Ala	Ser	Val	Thr 235	Ile	Ser	Asn	Asn	Ala 240
Lys	Val	Ser	Phe	Ile	Asp	Asn	Lys	Val	Thr		Ala	Ser	Ser	Ser	Thr

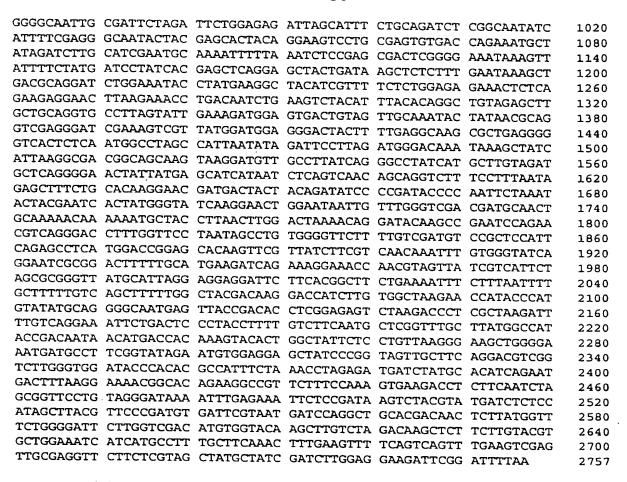
			•	245					250					255	
	,		260					265	Cys				270	Ser	Thr
	Thr	275					280					285	Phe		
	Thr 290					295					300				
305	Ala				310					315					320
	Thr			325					330					335	
	Ser		340					345					350		
		355					360					365			Gly
	Ser 370					375					380				
385	Phe				390					395					400
	Leu			405					410					415	
	Asn		420					425					430		
	Ser	435					440					445			
	Gly 450					455					460				
465	Thr				470					475					480
	Glu			485					490					495	
	Ser		500					505					510		
	Lys	515					520					525			
	Thr 530					535					540				
545					550					555					Thr 560
	Asp			565					570					575	
			580					585					590		Phe
		595					600					605			Ser
	610					615					620				Leu
625					630					635					Ala 640
	Trp			645					650					655	
			660					665					670		Gly
		675					680					685			Gln
Jüll	690	GIY	мц	Asp	Arg	695	ıyr	rne	val	Ala	Lys 700	Asn	Gln	Gly	Thr

705					710					715			Tyr		720
				725					730				Pro	735	
			740					745					Thr 750		
		755					760					765	Gly		_
	770					775					780		Pro		
785					790					795			Met		800
				805					810				Gly	815	Glu
			820					825					Leu 830		
		835					840					845	Thr		
	850					855					860		Pro		
865					870					875			Phe		880
				885					890				His	895	Cys
			900					905					Glu 910	Leu	_
Gly	Ser	Ser 915	Arg	Asn	Tyr	Asn	Val 920	Asp	Leu	Gly	Ala	Lys 925	Tyr	Gln	Phe

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2757 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

ATGAGATCGT	CTTTTTCCTT	GTTATTAATA	TCTTCATCTC	TAGCCTTTCC	TCTCTTAATG	60
AGTGTTTCTG	CAGATGCTGC	CGATCTCACA	TTAGGGAGTC	GTGACAGTTA	TAATGGTGAT	120
ACAAGCACCA	CAGAATTTAC	TCCTAAAGCG	GCAACTTCTG	ATGCTAGTGG	CACGACCTAT	180
ATTCTCGATG	GGGATGTCTC	GATAAGCCAA	GCAGGGAAAC	AAACGAGCTT	AACCACCIAI	240
עוד איז	A CA CTGCACC	3 3 3 TOTT 3 CO		AMACGAGCII	AACCACAAGI	240
COLLITICIA	ACACIGCAGG	AAATCTTACC	TTCTTAGGGA	ACGGATTTTC	TCTTCATTTT	300
GACAATATTA	TTTCGTCTAC	TGTTGCAGGT	GTTGTTGTTA	GCAATACAGC	AGCTTCTGGG	360
ATTACGAAAT	TCTCAGGATT	TTCAACTCTT	CGGATGCTTG	САССТССТАС	GACCACAGGT	420
AAAGGAGCCA	ΤΤΑΑΑΑΤΤΑΟ	CGATGGTCTG	CTCTTTTTT	CONTRACTOR	CACCACAGGI	
3300333300		COMIGGICIG	GIGITIGAGA	GTATAGGGAA	TCTTGACCAA	480
AATGAAAATG	CCTCTAGTGA	AAATGGGGGA	GCCATCAATA	CGAAGACTTT	GTCTTTGACT	540
GGGAGTACGC	GGTTTGTAGC	GTTCCTTGGC	AATAGCTCGT	CGCAACAAGG	GGGAGCGATC	600
TATGCTTCTG	GTGACTCTGT	GATTTCTGAG	AATCCACCAA	mommor a see	SSCREEN	
ACTICICATION	6161616161	CATTICICAG	MAIGCAGGAA	TCTTGAGCTT	CGGAAACAAC	660
AGIGCGACAA	CATCAGGAGG	CGCGATCTCT	GCTGAAGGGA	ACCTTGTGAT	CTCCAATAAC	720
CAAAATATCT		CTGCAAAGCA				780
AAAGCAGGGG	CCAACCCACA	CCCTA TOTAL) COCCOUNTY C	CCGGAGCIAI	IGATIGIAAC	700
		CCCTATCTTG	ACTCTTTCAG	GAAATGAGAG	CCTGCATTTT	840
CIGAATAACA	CAGCAGGAAA	TAGTGGAGGT	GCGATTTATA	CCAAAAAATT	GGTGTTATCC	900
TCAGGACGAG		ATTTTCTAAC				960
				COUNTRACTME	AJJAAALJJI	- U In 1



(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 918 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Met 1	Arg	Ser	Ser	Phe 5	Ser	Leu	Leu	Leu	Ile 10	Ser	Ser	Ser	Leu	Ala 15	Phe
Pro	Leu	Leu	Met 20	Ser	Val	Ser	Ala	Asp 25	Ala	Ala	Asp	Leu	Thr	Leu	Gly
Ser	Arg	Asp 35	Ser	Tyr	Asn	Gly	Asp 40	Thr	Ser	Thr	Thr	Glu 45	Phe	Thr	Pro
Lys	Ala 50	Ala	Thr	Ser	Asp	Ala 55	Ser	Gly	Thr	Thr	Tyr 60	Ile	Leu	Asp	Gly
Asp 65	Val	Ser	Ile	Ser	Gln 70	Ala	Gly	Lys	Gln	Thr 75	Ser	Leu	Thr	Thr	Ser 80
Cys	Phe	Ser	Asn	Thr 85	Ala	Gly	Asn	Leu	Thr 90	Phe	Leu	Gly	Asn	Gly 95	
Ser	Leu	His	Phe 100	Asp	Asn	Ile	Ile	Ser 105	Ser	Thr	Val	Ala	Gly	Val	Val

Val	Ser	Asn 115	Thr	Ala	Ala	Ser	Gly 120	Ile	Thr	Lys	Phe	Ser 125	Gly	Phe	Ser
Thr	Leu 130	Arg	Met	Leu	Ala	Ala 135		Arg	Thr	Thr	Gly 140		Gly	Ala	Ile
Lys 145	Ile	Thr	Asp	Gly	Leu 150	Val	Phe	Glu	Ser	Ile 155		Asn	Leu	Asp	
_	Glu	Asn	Ala	Ser 165		Glu	Asn	Gly			Ile	Asn	Thr		160 Thr
Leu	Ser	Leu	Thr		Ser	Thr	Arg		170 Val	·Ala	Phe	Leu	Gly	175 Asn	Ser
Ser	Ser	Gln 195		Gly	Gly	Ala		185 Tyr	Ala	Ser	Gly		190 Ser	Val	Ile
Ser			Ala	Gly	Ile		200 Ser	Phe	Gly	Asn		205 Ser	Ala	Thr	Thr
	210 Gly	Gly	Ala	Ile		215 Ala	Glu	Gly	Asn		220 Val	Ile	Ser	Asn	
225	_		~1	_,	230					235					240
				245					250				Gly	255	
			260					265					Leu 270		
		275					280					285	Gly		
Gly	Gly 290	Ala	Ile	Tyr	Thr	Lys 295	Lys	Leu	Val	Leu	Ser 300	Ser	Gly	Arg	Gly
Gly 305	Val	Leu	Phe	Ser	Asn 310	Asn	Lys	Ala	Ala	Asn 315	Ala	Thr	Pro	Lys	Gly 320
	Ala	Ile	Ala	Ile 325		Asp	Ser	Gly	Glu 330		Ser	Ile	Ser		
Leu	Gly	Asn	Ile 340		Phe	Glu	Gly			Thr	Ser	Thr	Thr	335 Gly	Ser
Pro	Ala		Val	Thr	Arg	Asn		345 Ile	Asp	Leu	Ala		350 Asn	Ala	Lys
Phe		355 Asn		Arg	Ala		360 Arg	Gly	Asn	Lys	Val	365 Ile	Phe	Tyr	Asp
Pro	370 Ile	Thr	Ser	Ser	Glv	375 Ala	Thr	Asp	Lvs	Len	380 Ser	Leu	Δen	Lve	Ala
385					390				-1-	395				-,5	400
Asp	Ala	Gly	Ser	Gly 405	Asn	Thr	Tyr	Glu	Gly 410		Ile	Val	Phe	Ser 415	Gly
Glu	Lys	Leu	Ser 420	Glu		Glu	Leu	Lys 425	Lys	Pro	Asp	Asn			Ser
Thr	Phe		Gln		Val	Glu		Ala		Gly	Ala			Leu	Lys
Asp	Gly	435 Val		Val	Val	Ala	440 Asn		Ile	Thr	Gln	445 Val		Gly	Ser
_	450					455					460				
Lys	Val	Val	Met	Asp			Thr	Thr	Phe	Glu	Ala	Ser	Ala	Glu	Gly
465					470					475					480
				485					490					495	Thr
			500					505					510		Leu
Ser	Gly	Pro 515		Met	Leu	Val	Asp 520		Gln	Gly	Asn	Tyr 525	Tyr		His
His	Asn 530		Ser	Gln	Gln	Gln 535	Val		Pro	Leu	Ile 540	Glu		Ser	Ala
Gln			Met	Thr	Thr			Tle	Pro	Δας			T10	Lau	Asn
545					550					555					560
Inr	ınr	AST	Hls	туг	GIY	Tyr	Gln	Gly	Thr	Gly	Ile	Ile	· Val	Trp	Val

				565					570					575	
		Ala	280					585					590	Thr	
		Tyr 595					600					605	Val		
	010	Trp				9 T D					620	Gln			
023		Ser			630					635					640
		Ala		045					650					666	Ser
		His	000					665					670	Phe	
		Glu 675					680					685			
	690	Asp				695					700				
,03		Ser			110					715					720
		Gly		/25					730					735	
		Gly	740					745					750		
		Val 755					760					765			
	,,,	Ala				//5					780				
/05		Thr			790					795					900
		Lys		805					810					915	
		Asn	020					825					930		
		Ser 835					840					845			
	930	Asp				855					860				
000		Thr			870					875					990
		Asn		885					890					995	
		Val	900			Gly	Ser	Ser 905	Arg	Ser	Tyr	Ala	Ile 910	Asp	Leu
GIĀ	GIÀ	Arg 915	rne	GIÀ	Phe										

- (2) INFORMATION FOR SEQ ID NO:13:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2787 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

	•					
ATGAAATCCT	CTCTTCATTG	GTTTGTAATC	TCGTCATCTT	TAGCACTTCC	CTTGTCACTA	60
AATTTCTCTG	CGTTTGCTGC	TGTTGTTGAA	ATCAATCTAG	GACCTACCAA	TAGCTTCTCT	120
GGACCAGGAA	CCTACACTCC	TCCAGCCCAA	ACAACAAATG	CAGATGGAAC	TATCTATAAT	180
CTAACAGGGG	ATGTCTCAAT	CACCAATGCA	GGATCTCCGA	CAGCTCTAAC	CGCTTCCTGC	240
TTTAAAGAAA	CTACTGGGAA	TCTTTCTTTC	CAAGGCCACG	GCTACCAATT	TCTCCTACAA	300
AATATCGATG	CGGGAGCGAA	CTGTACCTTT	ACCAATACAG	CTGCAAATAA	GCTTCTCTCC	360
TTTTCAGGAT	TCTCCTATTT	GTCACTAATA	CAAACCACGA	ATGCTACCAC	AGGAACAGGA	420
GCCATCAAGT	CCACAGGAGC	TTGTTCTATT	CAGTCGAACT	ATAGTTGCTA	CTTTGGCCAA	480
AACTTTTCTA	ATGACAATGG	AGGCGCCCTC	CAAGGCAGCT	CTATCAGTCT	ATCGCTAAAC	540
CCCAACCTAA	CGTTTGCCAA	AAACAAAGCA	ACGCAAAAAG	GGGGTGCCCT	CTATTCCACG	600
GGAGGGATTA	CAATTAACAA	TACGTTAAAC	TCAGCATCAT	TTTCTGAAAA	TACCGCGGCG	660
AACAATGGCG	GAGCCATTTA	CACGGAAGCT	AGCAGTTTTA	TTAGCAGCAA	CAAAGCAATT	720
AGCTTTATAA	ACAATAGTGT	GACCGCAACC	TCAGCTACAG	GGGGAGCCAT	TTACTGTAGT	780
AGTACATCAG	CCCCCAAACC	AGTCTTAACT	CTATCAGACA	ACGGGGAACT	GAACTTTATA	840
GGAAATACAG	CAATTACTAG	TGGTGGGGCG	ATTTATACTG	ACAATCTAGT	тСтттСттСт	900
GGAGGACCTA	CGCTTTTTAA	AAACAACTCT	GCTATAGATA	CTGCAGCTCC	CTTAGGAGGA	960
GCAATTGCGA	TTGCTGACTC	TGGATCTTTG	AGTCTTTCGG	CTCTTGGTGG	AGECATCACT	1020
TTTGAAGGAA	ACACAGTAGT	CAAAGGAGCT	TCTTCGAGTC	AGACCACTAC	CAGAAATTCT	1080
ATTAACATCG	GAAACACCAA	TGCTAAGATT	GTACAGCTGC	GAGCCTCTCA	ACCCAATACT	1140
ATCTACTTCT	ATGATCCTAT	AACAACTAAC	CATACTGCAG	CTCTCTCAGA	TECTETAAAC	1200
TTAAATGGTC	CTGACCTTGC	AGGGAATCCT	GCATATCAAG	GAACCATCGT	ATTTTCTCCA	1260
GAGAAGCTCT	CGGAAGCAGA	AGCTGCAGAA	GCTGATAATC	TCAAATCTAC	ATTICIOGA	
CCTCTAACTC	TTGCGGGAGG	GCAACTCTCT	CTTAAATCAG	GAGTCACTCT	ACTTCCTTAAC	1320
TCCTTTTCGC	AATCTCCGGG	CTCTACCCTC	CTCATGGATG	CAGGGACCAC	ATTACAAACC	1380
GCTGATGGGA	TCACTATCAA	TAATCTTGTT	CTCAATGTAG	ATTCCTTAAA	ACACACCAACC	1440 1500
AAGGCTACGC	TAAAAGCAAC	ACAAGCAAGT	CAGACAGTCA	CTTTATCTGG	ATCCCTCTCT	1560
CTTGTAGATC	CTTCTGGAAA	TGTCTACGAA	GATGTCTCTT	GGAATAACCC	TCAAGTCTTT	1620
TCTTGTCTCA	CTCTTACTGC	TGACGACCCC	GCGAATATTC	ACATCACAGA	CTTAGCTGCT	1680
GATCCCCTAG	AAAAAAATCC	TATCCATTGG	GGATACCAAG	GGAATTGGGC	ATTATCTTCC	1740
CAAGAGGATA	CTGCGACTAA	ATCCAAAGCA	GCGACTCTTA	CCTGGACAAA	AACAGGATAC	1800
AATCCGAATC	CTGAGCGTCG	TGGAACCTTA	GTTGCTAACA	CGCTATGGGG	ATCCTTTCTT	1860
GATGTGCGCT	CCATACAACA	GCTTGTAGCC	ACTAAAGTAC	GCCAATCTCA	AGAAACTCGC	1920
GGCATCTGGT	GTGAAGGGAT	CTCGAACTTC	TTCCATAAAG	ATAGCACGAA	GATAAATAAA	1980
GGTTTTCGCC	ACATAAGTGC	AGGTTATGTT	GTAGGAGCGA	CTACAACATT	AGCTTCTGAT	2040
AATCTTATCA	CTGCAGCCTT	CTGCCAATTA	TTCGGGAAAG	ATAGAGATCA	CTTTATAAAT	2100
AAAAATAGAG	CTTCTGCCTA	TGCAGCTTCT	CTCCATCTCC	AGCATCTAGC	GACCTTCTCT	2160
TCTCCAAGCT	TGTTACGCTA	CCTTCCTGGA	TCTGAAAGTG	AGCAGCCTGT	CCTCTTTCAT	2220
GCTCAGATCA	GCTATATCTA	TAGTAAAAAT	ACTATGAAAA	CCTATTACAC	CCAAGCACCA	2280
AAGGGAGAGA	GCTCGTGGTA	TAATGACGGT	TGCGCTCTGG	AACTTGCGAG	CTCCCTACCA	2340
CACACTGCTT	TÄAGCCATGA	GGGTCTCTTC	CACGCGTATT	TTCCTTTCAT	CAAAGTAGAA	2400
GCTTCGTACA	TACACCAAGA	TAGCTTCAAA	GAACGTAATA	CTACCTTGGT	ACCATCTTC	2460
GATAGCGGTG	ATTTAATTAA	CGTCTCTGTG	CCTATTGGAA	TTACCTTCGA	CACATTTCTCC	
AGAAACGAGC	GTGCGTCTTA	CGAAGCTACT	GTCATCTACG	TTGCCGATGT	CTATCCTCG	2520
AATCCTGACT	GCACGACAGC	TCTCCTAATC	AACAATACCT	CGTGGAAAAC	TACACCAACC	2580
AATCTCTCAA	GACAAGCTGG	TATCGGAAGA	GCAGGGATCT	TTTATGCCTT	CTCTCCNNNT	2640
CTTGAGGTCA	CAAGTAACCT	ATCTATGGAA	ATTCGTGGAT	CTTCACGCAG	CTACAAMI	2700
GATCTTGGAG	GTAAGTTCCA	GTTCTAA	COIGGAI	CIICACGCAG	CIACAAIGCA	2760
						2787

(2) INFORMATION FOR SEQ ID NO:14:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 928 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Met 1	Lys	Ser	Ser	Leu 5	His	Trp	Phe	Val	Ile 10	Ser	Ser	Ser	Leu	Ala 15	Leu
Pro	Leu	Ser	Leu 20	Asn	Phe	Ser	Ala	Phe 25		Ala	Val	Val	Glu 30	Ile	Asn
Leu	Gly	Pro 35	Thr	Asn	Ser	Phe	Ser 40	Gly	Pro	Gly	Thr	Tyr 45	Thr	Pro	Pro
	50					55					60			Gly	_
65					70					75				Ser	80
				85					90					Tyr 95	
			100					105					110	Thr	
		115					120					125		Leu	
	130					135					140			Lys	
145					150					155				Gly	160
				165					170					Ile 175	
			. 180					185					190	Thr	
		195					200					205		Asn	
	210					215					220			Gly	
225					230					235				Ala	240
				245					250					Gly 255	
			260					265					270	Leu	
	1	275					280					285		Ser	
	290		-			295					300			Pro	
305					310					315				Gly	320
				325					330					Leu 335	
			340					345					350	Ser	
		355					360					365		Asn	
	370					375					380			Phe	
385					390					395				Leu	400
				405					410					Thr 415	
			420					425					430	Ala	
Asn	Leu	Lys	Ser	Thr	Ile	Gln	Gln	Pro	Leu	Thr	Leu	Ala	Gly	Gly	Gln

		435					440								
Leu	Ser		Lve	Ser	Glv	V=1	440	I 011	W-1	N1 -	T	445	Phe		~1
	450		-75	-	Cly	455	1111	neu	vai	AIA	460	ser	Pne	ser	Gin
Ser	Pro	Gly	Ser	Thr	Leu		Met	Asp	Ala	Glv		Thr	Leu	Glu	Thr
465					470					475					480
Ala	Asp	Gly	Ile	Thr	Ile	Asn	Asn	Leu	Val	Leu	Asn	Val	Asp	Ser	Leu
T	01	m\	T	485			_		490					495	
гАг	GIU	inr	PAS	Lys	Ala	Thr	Leu	Lys 505	Ala	Thr	Gln	Ala	Ser	Gln	Thr
Val	Thr	Leu		Glv	Ser	I.e.i	Ser		1/2 l	700	Dro	Com	510 Gly	N	17- 1
		515					520	Lcu	Val	дел	FIO	525	Gry	ASII	vai
Tyr	Glu	Asp	Val	Ser	Trp	Asn	Asn	Pro	Gln	Val	Phe		Cys	Leu	Thr
	530					535					540				
Leu 545	Thr	Ala	Asp	Asp		Ala	Asn	Ile	His		Thr	Asp	Leu	Ala	Ala
	Pro	Leu	Glu	Luc	550	Dro	Tla	uia	m	555	m	01 -	Gly	_	560
nsp	110	Вси	Olu	565	ASII	PLO	TIE	HIS	570	GIY	Tyr	Gin	GIY	Asn 575	Trp
Ala	Leu	Ser	Trp	Gln	Glu	Asp	Thr	Ala		Lvs	Ser	Lvs	Ala		Thr
			580					585					590		
Leu	Thr	Trp	Thr	Lys	Thr	Gly		Asn	Pro	Asn	Pro	Glu	Arg	Arg	Gly
The	T 011	595	7 l -	7	m	.	600	~ 1	_			605			
1111	610	vai	AId	ASI	inr	615	Trp	Gly	Ser	Phe		Asp	Val	Arg	Ser
Ile		Gln	Leu	Val	Ala		Lvs	۷al	Ara	Gln	620 Ser	Gln	Glu	Th-	N
625					630					635					640
Gly	Ile	Trp	Cys	Glu	Gly	Ile	Ser	Asn	Phe	Phe	His	Lys	Asp	Ser	Thr
				645					650					655	
гÀг	TTE	Asn	Lys 660	GLY	Phe	Arg	His		Ser	Ala	Gly	Tyr	Val	Val	Gly
Ala	Thr	Thr		Leu	Ala	Ser	Asn	665	Lau	Tlo	The	717	670 Ala	Db -	-
		675					680	11311	пси	116	1111	685	міа	PHE	Cys
Gln	Leu	Phe	Gly	Lys	Asp	Arg	Asp	His	Phe	Ile	Asn		Asn	Arg	Ala
0 -	690	_			_	695					700				
705	Ala	Tyr	Ala	Ala	Ser 710	Leu	His	Leu	Gln		Leu	Ala	Thr	Leu	
	Pro	Ser	Leu	Leu		Tvr	ľ.eu	Pro	Gly	715	G) v	Co-	Glu	C1-	720
				725	5	-] -	LCu	110	730	361	GIU	ser	GIU	735	Pro
Val	Leu	Phe	Asp	Ala	Gln	Ile	Ser	Tyr		Tyr	Ser	Lys	Asn		Met
			740					745					750		
Lys	Thr	Tyr	Tyr	Thr	Gln	Ala	Pro	Lys	Gly	Glu	Ser		Trp	Tyr	Asn
Asp	Glv	755 Cvs	Ala	ī.eu	Glu	Len	760	80-	S-0-	T 0	D	765	Thr		_
	770	Cys	niu	ne u	GIU	775	Ala	ser	ser	Leu	780	HIS	Thr	Ala	Leu
Ser	His	Glu	Gly	Leu	Phe		Ala	Tyr	Phe	Pro		Ile	Lys	Val	Glu
785					790					795					800
Ala	Ser	Tyr	Ile	His	Gln	Asp	Ser	Phe		Glu	Arg	Asn	Thr	Thr	Leu
Val	λνα	502	Dha	805	C 0 x	C1	N	•	810			_		815	
Val	ALG	361	820	ASD	Set	GIY	ASP	825	ile	Asn	Val	Ser	Val	Pro	Ile
Gly	Ile	Thr		Glu	Arg	Phe	Ser		Asn	Glu	Ara	Δla	830 Ser	Tur	Glu
		835					840					845			
Ala	Thr	Val	Ile	Tyr	Val	Ala	Asp	Val	Tyr	Arg	Lys	Asn	Pro	Asp	Cys
	850					855					860				
865	ınr	ALA	ьeu	Leu	11e 870	Asn	Asn	Thr	Ser		Lys	Thr	Thr	Gly	
	Leu	Ser	Ara	Gln		Glv	Ile	Glv	Ara	875 Ala	Glv	Tle	Phe	ጥላታ፦	088
			,	885		- 1		1	890		J-7		- 11C	895	urq

(2) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2793 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ATGAAAATAC CCTT	GCACAA ACTCCTGATO	TCTTCGACTC	TTGTCACTCC	CATTCTATTG	60
	CGGAGC AGATGCTTCT				120
	TACTCC AAAATCTACA				180
	TATAAA CGATGCTGGC				240
	TGATCT GACATTTACT				300
	GAATGC AGGAGCTGC				360
	TAACCT TTCCTTCAT				420
	TTCTGC AGGAGCCTT				480
AGCCAAAACG. TCTC	CAATGA AGCTAATAA	AATGGCGGAG	CGATCACCAC	AAAAACTCTT	540
	TACCTC TTCTATAACO				600
GGAGCGATCT ATAG	CTCTGC GGCTGCAAG	TATTCAGGAA	ACACCGGCCA	GTTAGTCTTT	660
	SAGAAAC TGGGGGCGG				720
	CCTTTT CTTCTCTGG				780
	STGAAAA AACAGGAGAG				840
	CCGAGAA CTCTTCAGT				900
	TTGCTGG CCCTACCCT				960
	GCGCTAT TGCAATTGC				1020
	CGTTCCT TGGCAACAC				1080
	ACCTGGG ATCGTCAGC				1140
	CTATGA TCCGATTGC				1200
	CGGATAG CAACTCGCC				1260
	CTGCAGA TGAAGCGAA				1320
	PAGCCTC TGGAACCTT.				1380
	AGACTGA AGGCTCTAC				1440
	CTATCAG TCTTACCAA				1500
	CCATTGA AACAGCAGG				1560 -
	ATAGTAG CGGCAATTT				1620
	TGGTATT CACTGCTGC				1680
	CAGTACA AACTCCAGA				1740
	ACACATC AACTGCAAA				1800
TACAACCCTA ATC	CTGAGCG TAGAGCTTC	C GTAGTTCCCG	ATTCATTATG	GGCATCCTTT	1860
	CTCTACA GCAGATCAT				1920
CGAGGACTCT GGG	CATCAGG AACTGCGAA	T TTCTTCCATA	AGGATAAATC	AGGAACTAAC	1980
	ATAAAAG CTACGGCTA				2040
GAAAATATCT TCA	GTGTAGC TTTCTGCCA	G CTCTTCGGTA	AAGATAAAGA	CCTGTTTATA	2100
GTTGAAAATA CCT	CTCATAA CTATTTAGC	G TCGCTATACC	TGCAACATCG	AGCATTCCTA	2160
GGAGGACTTC CCA	TGCCCTC ATTTGGAAG	T ATCACCGACA	TGCTGAAAGA	TATTCCTCTC	2220
ATTTTGAATG CCC	AGCTAAG CTACAGCTA	C ACTAAAAATG	ATATGGATAC	TCGCTATACT	2280
	CTCAAGG TTCTTGGAC				2340
TCTCTGGCTC TAT	ATCTCCC TAAAGAAGC	A CCGTTCTTCC	AGGGATATTT	CCCCTTCTTA	2400

AAGTTCCAGG	CAGTCTACAG	CCGCCAACAA	AACTTTAAAG	AGAGTGGCGC	TGAAGCCCGT	2460
GCTTTTGATG	ATGGAGACCT	AGTGAACTGC	TCTATCCCTG	TCGGCATTCG	GTTAGAAAAA	2520
ATCTCCGAAG	ATGAAAAAA	TAATTTCGAG	ATTTCTCTAG	CCAACATTGG	TGATGTGTAT	2580
CGTAAAAATC	CCCGTTCGCG	TACTTCTCTA	ATGGTCAGTG	GAGCCTCTTG	GACTTCGCTA	2640
TGTAAAAACC	TCGCACGACA	AGCCTTCTTA	GCAAGTGCTG	GAAGCCATCT	GACTCTCTCC	2700
CCTCATGTAG	AACTCTCTGG	GGAAGCTGCT	TATGAGCTTC	GTGGCTCAGC	ACACATCTAC	2760
AATGTAGATT	GTGGGCTAAG	ATACTCATTC	TAG			2793

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 930 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

T				5					10		Ser			15	
			20					25			Asp		3.0	Leu	
		35					40				Thr	45			
	50					55					Leu 60				
65				•	70					75	Thr				RΛ
				85					90		Lys			95	
			100					105			Gly		110		
		115					120				Phe	125			
	130					135					Gly 140				
145					150					155	Gly				160
				165					170		Gly			175	Thr
			180					185			Ser		190	Phe	
		195					200				Tyr	205	Ser		
	210					215					Phe 220				
225					230					235	Ala				240
				245					250		Thr			255	
			260					265			Thr		270	Thr	
		275					280				Phe	285	Glu		
Ser	Val	Thr	Gln	Gly	Gly	Ala	Ile	Cys	Ala	His	Gly	Leu	Asp	Leu	Ser

	290					295					300				
Ala	Ala	Gly	Pro	Thr	Leu	Phe	Ser	Asn	Asn	Arg		Gly	Asn	Thr	Ala
305	•				310					315					320
Ala	Gly	Lys	Gly	Gly 325	Ala	Ile	Ala	Ile	Ala 330	Asp	Ser	Gly	Ser	Leu 335	Ser
Leu	Ser	Ala	Asn 340	Gln	Gly	Asp	Ile	Thr 345	Phe	Leu	Gly	Asn	Thr 350	Leu	Thr
Ser	Thr	Ser 355	Ala	Pro	Thr	Ser	Thr 360		Asn	Ala	Ile	Tyr 365	Leu	Gly	Ser
Ser	Ala 370	Lys	Ile	Thr	Asn	Leu 375		Ala	Ala	Gln	Gly 380		Ser	Ile	Tyr
Phe	Tyr	Asp	Pro	Ile	Ala		Asn	Thr	Thr	Glv		Ser	Asp	Val	ī.em
385					390					395					400
				405					410					Gly 415	
			420					425					430	Ala	
		435					440					445		Ser	
Thr	Leu 450	Ala	Leu	Lys	Gly	Asn 455	Val	Glu	Leu	Asp	Val 460	Asn	Gly	Phe	Thr
Gln 465	Thr	Glu	Gly	Ser	Thr 470	Leu	Leu	Met	Gln	Pro 475	Gly	Thr	Lys	Leu	Lys 480
Ala	Asp	Thr	Glu	Ala 485	Ile	Ser	Leu	Thr	Lys 490	Leu	Val	Val	Asp	Leu 495	Ser
Ala	Leu	Glu	Gly 500	Asn	Lys	Ser	Val	Ser 505	Ile	Glu	Thr	Ala	Gly 510	Ala	Asn
Lys	Thr	Ile 515	Thr	Leu	Thr	Ser	Pro 520		Val	Phe	Gln	Asp 525	Ser	Ser	Gly
Asn	Phe 530	Tyr	Glu	Ser	His	Thr 535		Asn	Gln	Ala	Phe 540	Thr	Gln	Pro	Leu
Val 545	Val	Phe	Thr	Ala	Ala 550		Ala	Ala	Ser	Asp 555		Tyr	Ile	Asp	Ala 560
Leu	Leu	Thr	Ser	Pro 565	Val	Gln	Thr	Pro	Glu 570		His	Tyr	Gly	Tyr 575	Gln
Gly	His	Trp	Glu 580	Ala	Thr	Trp	Ala	Asp 585		Ser	Thr	Ala	Lys 590	Ser	Gly
Thr	Меt	Thr 595	Trp	Val	Thr	Thr	Gly 600		Asn	Pro	Asn	Pro 605		Arg	Arg
Ala	Ser 610	Val	'Val	Pro	Asp	Ser 615		Trp	Ala	Ser	Phe 620	Thr	Asp	Ile	Arg
Thr 625	Leu	Gln	Gln	Ile	Met 630		Ser	Gln	Ala	Asn 635	Ser	Ile	Tyr	Gln	Gln 640
				645					650					Asp 655	Lys
			660					665					670	Ile	
		675					680					685		Ala	
	690					695					700			Asn	
705					710					715				Phe	720
				725					730					Leu 735	Lys
Asp	Ile	Pro	740	Ile	Leu	Asn	Ala	Gln 745		Ser	Tyr	Ser	Tyr 750	Thr	Lys

		755				Tyr	760					765			
	770					Ala 775					780				
785					790	Pro				795					800
				805		Ser			810					815	Gly
			820			Asp		825					830		
		835				Glu	840					845			
	850					Asn 855					860				
865					870	Met				875					880
				885		Gln			890					895	
			900			Val		905					910		
		Gly 915	Ser	Ala	His	Ile	Tyr 920	Asn	Val	Asp	Cys	Gly 925	Leu	Arg	Tyr
Ser	Phe 930														

(2) INFORMATION FOR SEQ ID NO:17:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 840 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

CAACACAANA MAAGGERAGE					
GAAGACAATA TAAGGTACCG	TCATAACAGC	GGGGGTTATG	CACTAGGGAT	CACAGCAACA	60
ACTCCTGCCG AGGATCAGCT	TACTTTTGCC	TTCTGCCAGC	TCTTTGCTAG	AGATCGCAAT	120
CATATTACAG GTAAGAACCA	CGGAGATACT	TACGGTGCCT	CALALCAVALAL	CCACCATACA	180
GAAGGGCTCT TCGACATCGC	CAATTTCCTC	TGGGGAAAAG	CAACCCGAGC	TCCCTCCCTC	
CECOMONO. A. M. M. C.		100001111110	CAACCCGAGC	1000100010	240
CTCTCTGAGA TCTCCCAGAT	CATTCCTTTA	TCGTTCGATG	CTAAATTCAG	TTATCTCCAT	300
ACAGACAACC ACATGAAGAC	ATATTATACC	GATAACTCTA	TCATCAAGGG	TTCTTGGAGA	360
AACGATGCCT TCTGTGCAGA	TCTTGGAGCT	AGCCTGCCTT	TTGTTATTTC	CGTTCCGTAT	420
CTTCTCANAC AACTCCAACC	mmmmamaa a a	~~~		COLICCOIAI	420
CTTCTGAAAG AAGTCGAACC	TTTTGTCAAA	GTACAGTATA	TCTATGCGCA	TCAGCAAGAC	480
TTCTACGAGC GTCATGCTGA	AGGACGCGCT	TTCAATAAAA	GCGAGCTTAT	CAACGTAGAG	540
ATTCCTATAG GCGTCACCTT	CGAAAGAGAC	TCAAAATCAG	AAAAGGGAAC	TTACCATCTT	600
ልርጥርጥጥ አጥርጥ አጥአጥአርመረር እ	MCCMM2 ccc2			TINCOMICII	000
ACTCTTATGT ATATACTCGA	TGCTTACCGA	CGCAATCCTA	AATGTCAAAC	TTCCCTAATA	660
GCTAGCGATG CTAACTGGAT	GGCCTATGGT	ACCAACCTCG	CACGACAAGG	TTTTTCTGTT	720
CGTGCTGCGA ACCATTTCCA	ACTCA ACCCC	CACAMOGRAAA	m.c		•
Chicago Accarrica	AGIGAACCCC	CACAIGGAAA	TUTTCGGTCA	ATTCGCTTTT	780
GAAGTACGAA GTTCTTCACG	TAATTATAAT	ACAAACCTAG	GCTCTAAGTT	TTGTTTCTAG	840
					340

(2) INFORMATION FOR SEQ ID NO:18:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 279 amino acids
 - (B) TYPE: amino acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Glu Asp Asn Ile Arg Tyr Arg His Asn Ser Gly Gly Tyr Ala Leu Gly Ile Thr Ala Thr Thr Pro Ala Glu Asp Gln Leu Thr Phe Ala Phe Cys Gln Leu Phe Ala Arg Asp Arg Asn His Ile Thr Gly Lys Asn His Gly 40 Asp Thr Tyr Gly Ala Ser Leu Tyr Phe His His Thr Glu Gly Leu Phe 55 Asp Ile Ala Asn Phe Leu Trp Gly Lys Ala Thr Arg Ala Pro Trp Val Leu Ser Glu Ile Ser Gln Ile Ile Pro Leu Ser Phe Asp Ala Lys Phe Ser Tyr Leu His Thr Asp Asn His Met Lys Thr Tyr Tyr Thr Asp Asn 105 Ser Ile Ile Lys Gly Ser Trp Arg Asn Asp Ala Phe Cys Ala Asp Leu 120 125 Gly Ala Ser Leu Pro Phe Val Ile Ser Val Pro Tyr Leu Leu Lys Glu 135 Val Glu Pro Phe Val Lys Val Gln Tyr Ile Tyr Ala His Gln Gln Asp 150 155 Phe Tyr Glu Arg His Ala Glu Gly Arg Ala Phe Asn Lys Ser Glu Leu 165 170 Ile Asn Val Glu Ile Pro Ile Gly Val Thr Phe Glu Arg Asp Ser Lys 185 Ser Glu Lys Gly Thr Tyr Asp Leu Thr Leu Met Tyr Ile Leu Asp Ala Tyr Arg Arg Asn Pro Lys Cys Gln Thr Ser Leu Ile Ala Ser Asp Ala 215 Asn Trp Met Ala Tyr Gly Thr Asn Leu Ala Arg Gln Gly Phe Ser Val 230 235 Arg Ala Ala Asn His Phe Gln Val Asn Pro His Met Glu Ile Phe Gly 245 250 Gln Phe Ala Phe Glu Val Arg Ser Ser Ser Arg Asn Tyr Asn Thr Asn 260 Leu Gly Ser Lys Phe Cys Phe 275

- (2) INFORMATION FOR SEQ ID NO:19:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1545 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATGACCATAC TTCGAAATTT TCTTACCTGC TCGGCTTTAT TCCTCGCTCT CCCTGCAGCA

GCACAAGTTG	TATATCTTCA	TGAAAGTGAT	GGTTATAACG	GTGCTATCAA	TAATAAAAGC	120
TTAGAACCTA		TTATCCAGAA	GGAACTTCTT	ACATCTTTCT	AGATGACGTG	180
AGGATTTĊCA	ACGTTAAGCA	TGATCAAGAA	GATGCTGGGG	TTTTTTATAAA	TCGATCTGGG	240
AATCTTTTTT	TCATGGGCAA	CCGTTGCAAC	TTCACTTTTC	ACAACCTTAT	GACCGAGGGT	300
TTTGGCGCTG	CCATTTCGAA	CCGCGTTGGA	GACACCACTC	TCACTCTCTC	TAATTTTTCT	360
TACTTAACGT	TCACCTCAGC	ACCTCTACTA	CCTCAAGGAC	AAGGAGCGAT	TTATAGTCTT	420
GGTTCCGTGA	TGATCGAAAA	TAGTGAGGAA	GTGACTTTCT	GTGGGAACTA	CTCTTCGTGG	480
AGTGGAGCTG	CGATTTATAC	TCCCTACCTT	TTAGGTTCTA	AGGCGAGTCG	TCCTTCAGTA	540
AATCTCAGCG	GGAACCGCTA	CCTGGTGTTT	AGAGACTATG	TGAGCCAAGG	TTATGGCGGC	600
GCCGTATCTA	CCCACAATCT	CACACTCACG	ACTCGAGGAC	CTTCGTGTTT	TGAAAATAAT	660
CATGCTTATC	ATGACGTGAA	TAGTAATGGA	GGAGCCATTG	CCATTGCTCC	TGGAGGATCG	720
ATCTCTATAT	CCGTGAAAAG	CGGAGATCTC	ATCTTCAAAG	GAAATACAGC	ATCACAAGAC	780
GGAAATACAA	TACACAACTC	CATCCATCTG	CAATCTGGAG	CACAGTTTAA	GAACCTACGT	840
GCTGTTTCAG	AATCCGGAGT	TTATTTCTAT	GATCCTATAA	GCCATAGCGA	GTCGCATAAA	900
ATTACAGATC	TTGTAATCAA	TGCTCCTGAA	GGAAAGGAAA	CTTATGAAGG	AACAATTAGC	960
TTCTCAGGAC	TATGCCTGGA	0 0		AAAATCTTAC	TTCCACAATC	1020
CTACAAGATG		AGGAGGAACT		CGGATGGGGT	TACCTTGCAA	1080
CTGCATTCTT	TTAAGCAGGA	AGCAAGCTCT	ACGCTTACTA	TGTCTCCAGG	AACCACTCTG	1140
CTCTGCTCAG	GAGATGCTCG	GGTTCAGAAT	CTGCACATCC	TGATTGAAGA	TACCGACAAC	1200
TTTGTTCCTG	TAAGGATTCG	CGCCGAGGAC	AAGGATGCTC	TTGTCTCATT	AGAAAAACTT	1260
AAAGTTGCCT	TTGAGGCTTA	TTGGTCCGTC	TATGACTTTC	CTCAATTTAA	GGAAGCCTTT	1320
ACGATTCCTC	TTCTTGAACT	TCTAGGGCCT	TCTTTTGACA	GTCTTCTCCT	AGGGGAGACC	1380
ACTTTGGAGA	0.2.0001101	CACAACAGAG	AATGACGCCG	TTCGAGGTTT	CTGGTCCCTA	1440
AGCTGGGAAG	AGTACCCCCC			GGATCACACC	AACTAAGAAA	1500
ACTGTTTTCC	TCACTTGGAA	TCCTGAGATC	ACTTCTACGC	CATAA		1545

(2) INFORMATION FOR SEQ ID NO:20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 514 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met 1	Thr	Ile	Leu	Arg 5	Asn	Phe	Leu	Thr	Cys 10	Ser	Ala	Leu	Phe	Leu 15	Ala
Leu	Pro	Ala	Ala 20	Ala	Gln	Val	Val	Tyr 25	Leu	His	Glu	Ser	Asp 30	Gly	Tyr
Asn	Gly	Ala 35	Ile	Asn	Asn	Lys	Ser 40	Leu	Glu	Pro	Lys	Ile 45	Thr	Cys	Tyr
Pro	Glu 50	Gly	Thr	Ser	Tyr	Ile 55	Phe	Leu	Asp	Asp	Val 60	Arg	Ile	Ser	Asn
Val 65	Lys	His	Asp	Gln	Glu 70	Asp	Ala	Gly	Val	Phe 75	Ile	Asn	Arg	Ser	Gly 80
Asn	Leu	Phe	Phe	Met 85	Gly	Asn	Arg	Cys	Asn 90	Phe	Thr	Phe	His	Asn	Leu
Met	Thr	Glu	Gly 100	Phe	Gly	Ala	Ala	Ile 105	Ser	Asn	Arg	Val	Gly 110		Thr
Thr	Leu	Thr 115	Leu	Ser	Asn	Phe	Ser 120	Tyr	Leu	Thr	Phe	Thr 125		Ala	Pro
Leu	Leu 130	Pro	Gln	Gly	Gln	Gly 135	Ala	Ile	Tyr	Ser	Leu 140		Ser	Val	Met
Ile	${\tt Glu}$	Asn	Ser	Glu	Glu	Val	Thr	Phe	Cys	Glv		Tvr	Ser	Ser	Trn

145					150					155					160
Ser	Gly	Ala	Ala	Ile		Thr	Pro	Tvr	ī.eu	Len	Glv	Sar	T	Ala	160
	•			165	- 1 -			- 1 -	170	<u> LCu</u>	Gry	Ser	гÀ2	175	Ser
Arg	Pro	Ser	Val	Asn	Leu	Ser	Glv	Asn		Tur	Ι. Α. 1.	V-1	Dho	Arg	7
			180					185	nr 9	LYL	Leu	vai		Arg	Asp
Tvr	Val	Ser	Gln	Glv	Tvr	Glv	Glv		V-1	80~	The	II i a	190	Leu	m)
2		195		1	- 1 -	CI	200	ALG	vai	251	TILL		ASI	Leu	Inr
Leu	Thr		Ara	Glv	Pro	Ser		Dhe	G1.,	700	>	205	21-	Tyr	
	210		5	<i>I</i>		215	Cys	- 116	GIU	ASII	220	HIS	Ala	Tyr	HIS
asp	Val	Asn	Ser	Asn	Glv		Δla	Tla	λ l ¬	T10	220	D	G1	Gly	_
225					230	Cry	AI u	116	MIG	235	Ald	PFO	GIÀ	GLY	
	Ser	Ile	Ser	٧a١		Ser	Glv	Acn	Lau	Z33	Dho	*	01	Asn	240
				245	2,5	001	CLY	μsρ	250	116	PHE	Lys	GIY		Thr
Ala	Ser	Gln	Asp		Δsn	Thr	Tla	Цic		C	T1.	772 -	. .	255 Gln	_
		•	260	4 - <i>y</i>		1111	110	265	ASII	Sei	TIE	HIS		GIN	Ser
Glv	Ala	Gln		Lvs	Δsn	T.eu	Δνα		1/21	C	C1	0	270	Val	-
1		275		- , 5		ncu.	280	MIG	vaı	ser	Gru		GIY	vai	Tyr
Phe	Tvr		Pro	Ile	Ser	His		Glu	Sar	uia	T	285	mb	Asp	.
	290				001	295	361	GIU	ser	nis	300	iie	Thr	Asp	Leu
Val	Ile	Asn	Ala	Pro	Glu		Lvs	Glu	Thr	Tire	C1	C1	mb	Ile	0
305					310	,	~, J	014	1111	315	GIU	GLY	IHL	TIE	
Phe	Ser	Gly	Leu	Cys		Asp	Asp	His	Glu	Val	Cve	Δ1 =	Cl.	Asn	320
		•		325					330	• • • •	Cys	AIG	Gra	335	rea
Thr	Ser	Thr	Ile	Leu	Gln	Asp	Val	Thr		Ala	Glv	Glv	Thr	Leu	Ser
			340					345					350		
Leu	Ser	Asp	Gly	Val	Thr	Leu	Gln	Leu	His	Ser	Phe	Lvs	Gln	Glu	Ala
		355					360					365			
Ser	Ser	Thr	Leu	Thr	Met	Ser	Pro	Gly	Thr	Thr	Leu	Leu	Cys	Ser	Glv
	370					375					380				
Asp	Ala	Arg	Val	Gln	Asn	Leu	His	Ile	Leu	Ile	Glu	Asp	Thr	Asp	Asn
385					390					395					400
Phe	Val	Pro	Val	Arg	Ile	Arg	Ala	Glu	Asp	Lys	Asp	Ala	Leu	Val	Ser
				405					410					415	
Leu	Glu	Lys	Leu	Lys	Val	Ala	Phe	Glu	Ala	Tyr	Trp	Ser	Val	Tyr	Asp
			420					425					430		
Phe	Pro	Gln	Phe	Lys	Glu	Ala	Phe	Thr	Ile	Pro	Leu	Leu	Glu	Leu	Leu
6 1	_	435		_	_ 0		440					445			
GIY	Pro	Ser	Phe	Asp	Ser	Leu	Leu	Leu	Gly	Glu	Thr	Thr	Leu	Glu	Arg
The sea	450	**- 1	m1.		~ .	455					460				
105	GIN	vai	Thr	Thr	Glu	Asn	Asp	Ala	Val	Arg	Gly	Phe	Trp	Ser	Leu
465	m	G1	01.	_	470	_	_			475					480
ser	ırp	GIU	GIU	Tyr	Pro	Pro	Ser	Leu		Lys	Asp	Arg	Arg	Ile	Thr
D~~	Th	T	T	485	** - 3	ο,			490					495	
P10	IUL	гÀЗ	FOO	inr	val	Phe	Leu		Trp	Asn	Pro	Glu	Ile	Thr	Ser
Th∽	Pro		500					505					510		
THE	FIO														

(2) INFORMATION FOR SEQ ID NO:21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 787 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

ATGAAAACGT	CTATTCGTAA	GTTCTTAATT	TCTACCACAC	TGGCGCCATG	TTTTGCTTCA	60
ACAGCGTTTA	CTGTAGAAGT	TATCATGCCT	TCCGAGAACT	TTGATGGATC	GAGTGGGAAG	120
ATTTTTCCTT	ACACAACACT	TTCTGATCCT	AGAGGGACAC	TCTGTATTTT	TTCAGGGGAT	180
CTCTACATTG	CGAATCTTGA	TAATGCCATA	TCCAGAACCT	CTTCCAGTTG	CTTTAGCAAT	240
AGGGCGGGAG	CACTACAAAT	CTTAGGAAAA	GGTGGGGTTT	TCTCCTTCTT	AAATATCCGT	300
TCTTCAGCTG	ACGGAGCCGC	GATTAGTAGT	GTAATCACCC	AAAATCCTGA	ACTATGTCCC	360
TTGAGTTTTT	CAGGATTTAG	TCAGATGATC	TTCGATAACT	GTGAATCTTT	GACTTCAGAT	420
ACCTCAGCGA	GTAATGTCAT	ACCTCACGCA	TCGGCGATTT	ACGCTACAAC	GCCCATGCTC	480
TTTACAAACA	ATGACTCCAT	ACTATTCCAA	TACAACCGTT	CTGCAGGATT	TGGAGCTGCC	540
ATTCGAGGCA	CAAGCATCAC	AATAGAAAAT	ACGAAAAAGA	GCCTTCTCTT	TAATGGTAAT	600
GGATCCATCT	CTAATGGAGG	GGCCCTCACG	GGATCTGCAG	CGATCAACCT	CATCAACAAT	660
AGCGCTCCTG	TGATTTTCTC	AACGAATGCT	ACAGGGATCT	ATGGTGGGC	TATTTACCTT	720
	CTATGCTCAC	CTCTGGGAAC	CTCTCAGGAG	TCTTGTTCGT	TTATAATAGC	780
TCGCGCT						787

(2) INFORMATION FOR SEQ ID NO:22:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 262 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

1				5		Lys			10					15	
			20			Phe		25					30		
		35		•		Gly	40					45			
	50					Cys 55					60				
65					70	Ser				75					80
				85		Ile			90					95	Phe
			100			Ala		105					110		
		115				Cys	120					125			
	130					Glu 135					140	Thr			
Asn 145	Val	Ile	Pro	His	Ala 150	Ser	Ala	Ile	Tyr	Ala 155	Thr	Thr	Pro	Met	Leu 160
Phe	Thr	Asn	Asn	Asp 165	Ser	Ile	Leu	Phe	Gln 170	Tyr	Asn	Arg	Ser	Ala 175	Gly
Phe	Gly	Ala	Ala 180	Ile	Arg	Gly	Thr	Ser 185	Ile	Thr	Ile	Glu	Asn 190	Thr	Lys
Lys	Ser	Leu 195	Leu	Phe	Asn	Gly	Asn 200	Gly	Ser	Ile	Ser	Asn 205	Gly	Gly	Ala
Leu	Thr 210	Gly	Ser	Ala	Ala	Ile 215	Asn	Leu	Ile	Asn	Asn 220	Ser	Ala	Pro	Val

 1le
 Phe
 Ser
 Thr
 Asn
 Ala
 Thr
 Gly
 Ile
 Tyr
 Gly
 Gly
 Ala
 Ile
 Tyr
 Leu

 225
 1
 230
 230
 235
 1
 240
 240

 Thr
 Gly
 Gly
 Asn
 Leu
 Ser
 Gly
 Val
 Leu
 Phe

 245
 250
 250
 255
 255
 255
 Yal
 Yal</

(2) INFORMATION FOR SEQ ID NO:23:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2838 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Genomic DNA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

ATGAAGACTT	CAGTTTCTAT	GTTGTTGGCC	CTGCTTTGCT	CGGGGGCTAG	CTCTATTGTA	60
CTCCATGCCG	CAACCACTCC	ACTAAATCCT	GAAGATGGGT	TTATTGGGGA	GGGCAATACA	120
AATACTTTTT	CTCCGAAATC	TACAACGGAT	GCTGCAGGAA	CTACCTACTC	TCTCACAGGA	180
GAGGTTCTGT	TTATAGATCC	GGGGAAAGGT	GGTTCAATTA	CAGGAACTTG	CTTTGTAGAA	240
ACTGCTGGCG	ATCTTACATT	TTTAGGTAAT	GGAAATACCC	TAAAGTTCCT	GTCGGTAGAT	300
GCAGGTGCTA	ATATCGCGGT	TGCTCATGTA	CAAGGAAGTA	AGAATTTAAG	CTTCACAGAT	360
TTCCTTTCTC	TGGTGATCAC	AGAATCTCCA	AAATCCGCTG	TTAGTACAGG	AAAAGGTAGC	420
CTAGTCAGTT	CAGGTGCAGT	CCAACTGCAA	GATATAAACA	CTCTAGTTCT	TACAAGCAAT	480
GCCTCTGTCG	AAGATGGTGG	CGTGATTAAA	GGAAACTCCT	GCTTGATTCA	GGGAATCAAA	540
AATAGTGCGA	TTTTTGGACA	AAATACATCT	TCGAAAAAAG	GAGGGGCGAT	CTCCACGACT	600
CAAGGACTCA	CCATAGAGAA	TAACTTAGGG	ACGCTAAAGT	TCAATGAAAA	CAAAGCAGTG	660
ACCTCAGGAG	GCGCCTTAGA	TTTAGGAGCC	GCGTCTACAT	TCACTGCGAA	CCATGAGTTG	720
ATATTTTCAC	AAAATAAGAC	TTCTGGGAAT	GCTGCAAATG	GCGGAGCCAT	AAATTGCTCA	780
GGCGACCTAA	CATTTACTGA	TAACACTTCT	TTGTTACTTC	AAGAAAATAG	CACAATGCAG	840
GATGGTGGAG	CTTTGTGTAG	CACAGGAACC	ATAAGCATTA	CCGGTAGTGA	TTCTATCAAT	900
GTGATAGGAA	ATACTTCAGG	ACAAAAAGGA	GGAGCGATTT	CTGCAGCTTC	TCTCAAGATT	960
TTGGGAGGGC	AGGGAGGCGC	TCTCTTTTCT	AATAACGTAG	TGACTCATGC	CACCCCTCTA	1020
GGAGGTGCCA	TTTTTATCAA	CACAGGAGGA	TCCTTGCAGC	TCTTCACTCA	AGGAGGGGAT	1080
ATCGTATTCG	AGGGGAATCA	GGTCACTACA	ACAGCTCCAA	ATGCTACCAC	TAAGAGAAAT	1140
GTAATTCACC	TCGAGAGCAC	CGCGAAGTGG	ACGGGACTTG	CTGCAAGTCA	AGGTAACGCT	1200
ATCTATTTCT	ATGATCCCAT	TACCACCAAC	GATACGGGAG	CAAGCGATAA	CTTACGTATC	1260
AATGAGGTCA	GTGCAAATCA	AAAGCTCTCG	GGATCTATAG	TATTTTCTGG	AGAGAGATTG	1320
TCGACAGCAG	AAGCTATAGC	TGAAAATCTT	ACTTCGAGGA	TCAACCAGCC	TGTCACTTTA	1380
GTAGAGGGGA	GCTTAGAACT	TAAACAGGGA	GTGACCTTGA	TCACACAAGG	ATTCTCGCAG	1440
GAGCCAGAAT	CCACGCTTCT	TTTGGATTTG	GGGACCTCAT	TACAAGCTTC	TACAGAAGAT	1500
ATCGTCATCA	CAAATTCATC	TATAAATGCC	GATACCATTT	ACGGAAAGAA	TCCAATCAAT	1560
ATTGTAGCTT	CAGCAGCGAA	TAAGAACATT	ACCCTAACAG	GAACCTTAGC	ACTTGTAAAT	1620
GCAGATGGAG	CTTTGTATGA	GAACCATACC	TTGCAAGACT	CTCAAGATTA	TAGCTTTGTA	1680
AAGTTATCTC	CAGGAGCGGG	AGGGACTATA	ATTACTCAAG	ATGCTTCTCA	GAAGCTTCTT	1740
GAAGTAGCTC	CTTCTAGACC	ACATTATGGC	TATCAAGGAC	ATTGGAATGT	GCAAGTCATC	1800
CCAGGAACGG	GAACTCAACC	GAGCCAGGCA	AATTTAGAAT	GGGTGCGGAC	AGGATACCTT	1860
CCGAATCCCG	AACGGCAAGG	ATTTTTAGTT	CCCAATAGCC	TGTGGGGTTC	TTTTGTTGAT	1920
CAGCGTGCTA	TCCAAGAAAT	CATGGTAAAT	AGTAGCCAAA	TCTTATGTCA	GGAACGGGGA	1980
GTCTGGGGAG	CTGGAATTGC	TAATTTCCTA	CATAGAGATA	AAATTAATGA	GCACGGCTAT	2040
CGCCATAGCG	GTGTCGGTTA	TCTTGTGGGA	GTTGGCACTC	ATGCTTTTTC	TGATGCTACG	2100
ATAAATGCGG	CTTTTTGCCA	GCTCTTCAGT	AGAGATAAAG	ACTACGTAGT	ATCCAAAAAT	2160
CATGGAACTA	GCTACTCAGG	GGTCGTATTT	CTTGAGGATA	CCCTAGAGTT	TAGAAGTCCA	2220
CAGGGATTCT	ATACTGATAG	CTCCTCAGAA	GCTTGCTGTA	ACCAAGTCGT	CACTATAGAT	2280

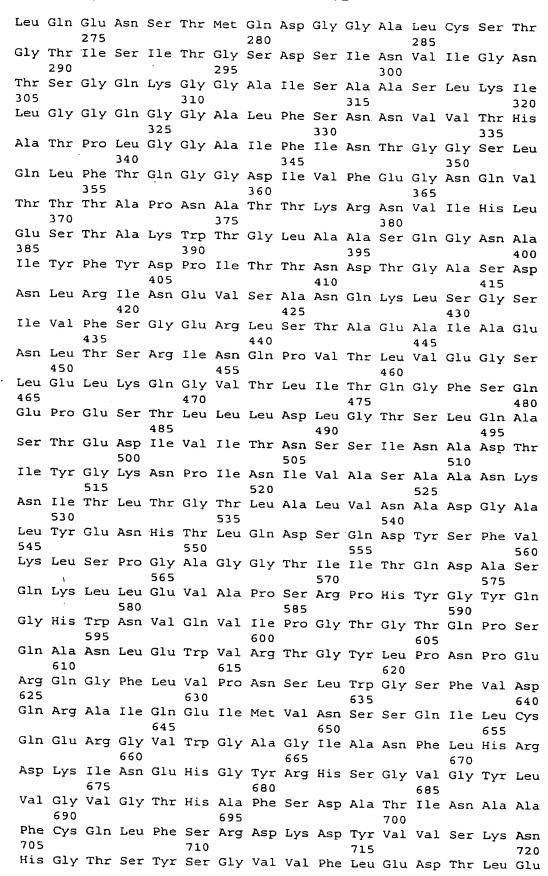
ATGCAGTTGT	CTTACAGCCA	TAGAAATAAT	GATATGAAAA	CCAAATACAC	GACATATCCA	2340
GAAGCTCAGG	GATCTTGGGC	AAATGATGTT	TTTGGTCTTG	AGTTTGGAGC	GACTACATAC	2400
TACTACCCTA	ACAGTACTTT	TTTATTTGAT	TACTACTCTC	CGTTTCTCAG	GCTGCAGTGC	2460
ACCTATGCTC	ACCAGGAAGA	CTTCAAAGAG	ACAGGAGGTG	AGGTTCGTCA	CTTTACTAGC	2520
GGAGATCTTT	TCAATTTAGC	AGTTCCTATT	GGCGTGAAGT	TTGAGAGATT	TTCAGACTGT	2580
AAAAGGGGAT	CTTATGAACT	TACCCTTGCT	TATGTTCCTG	ATGTGATTCG	CAAAGATCCC	2640
AAGAGCACGG	CAACATTGGC	TAGTGGAGCT	ACGTGGAGCA	CCCACGGAAA	CAATCTCTCC	2700
AGACAAGGAT	TACAACTGCG	TTTAGGGAAC	CACTGTCTCA	TAAATCCTGG	AATTGAGGTG	2760
TTCAGTCACG	GAGCTATTGA	ATTGCGGGGA	TCCTCTCGTA	ATTATAACAT	CAATCTCGGG	2820
GGTAAATACC	GATTTTAA					2838

(2) INFORMATION FOR SEQ ID NO:24:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 946 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

1				5					10					Gly 15	
			20					25					30	Glu	_
Gly	Phe	Ile 35	Gly	Glu	Gly	Asn	Thr 40	Asn	Thr	Phe	Ser	Pro 45	Lys	Ser	Thr
Thr	Asp 50	Ala	Ala	Gly	Thr	Thr 55	Tyr	Ser	Leu	Thr	Gly 60	Glu	Val	Leu	Phe
Ile 65	Asp	Pro	Gly	Lys	Gly 70	Gly	Ser	Ile	Thr	Gly 75	Thr	Cys	Phe	Val	Glu 80
				85					90					Lys 95	
Leu	Ser	Val	Asp 100	Ala	Gly	Ala	Asn	Ile 105	Ala	Val	Ala	His	Val 110	Gln	Gly
		115					120					125		Thr	
Ser	Pro 130	Lys	Ser	Ala	Val	Ser 135	Thr	Gly	Lys	Gly	Ser 140	Leu	Val	Ser	Ser
Gly 145	Ala	Val	Gln	Leu	Gln 150	Asp	Ile	Asn	Thr	Leu 155	Val	Leu	Thr	Ser	Asn 160
Ala	Ser	Val	Glu	Asp 165	Gly	Gly	Val	Ile	Lys 170	Gly	Asn	Ser	Cys	Leu 175	Ile
Gln	Gly	Ile	Lys 180	Asn	Ser	Ala	Ile	Phe 185	Gly	Gln	Asn	Thr	Ser 190	Ser	Lys
Lys	Gly	Gly 195	Ala	Ile	Ser	Thr	Thr 200	Gln	Gly	Leu	Thr	Ile 205	Glu	Asn	Asn
Leu	Gly 210	Thr	Leu	Lys	Phe	Asn 215	Glu	Asn	Lys	Ala	Val 220	Thr	Ser	Gly	Gly
Ala 225	Leu	Asp	Leu	Gly	Ala 230	Ala	Ser	Thr	Phe	Thr 235	Ala	Asn	His	Glu	Leu 240
Ile	Phe	Ser	Glņ	Asn 245	Lys	Thr	Ser	Gly	Asn 250	Ala	Ala	Asn	Gly	Gly 255	Ala
Ile	Asn	Cys	Ser 260	Gly	Asp	Leu	Thr	Phe 265	Thr	Asp	Asn	Thr	Ser 270	Leu	Leu



				725					730					735	
			740					745					750	Ala	
		755					760					765	Ser	His	
	770					775					780			Gln	_
785					790					795				Thr	800
				805					810					Phe 815	
			820		-		•	825					830	Thr	_
		835					840					845		Ala	
	850					855			-		850			Gly	
865					870				_	8.75				Asp	880
Lys	Ser	Thr	Ala	Thr 885	Leu	Ala	Ser	Gly	Ala 890	Thr	Trp	Ser	Thr	His 895	Gly
			900					905			•		910	His	
		915					920					925		Glu	
Arg Phe	Gly 930	Ser	Ser	Arg	Asn	Tyr 935	Asn	Ile	Asn	Leu	Gly 940	Gly	Lys	Tyr	Arg
945															

(2) INFORMATION FOR SEQ ID NO:25:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3000 base pairs
 - (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: Coding Sequence
- (B) LOCATION: 259...3000
- (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

ATCAGGTGAT AAAAGT	CCT CGTTAGCTA	G TGACTGTAGG	TGACATGAGA AAGCTAACAC	60
GGAGGAAACT AAAACC	CAAG GAATCGAAG	T CTTCATGGTA	ATGCTTTTGT TTTTTAGAGA	120
ACTATTCGCA TCAATAT	TAGA AACAAAATA	A GTAAATCAAG	TTAAAGATGA CAAAACAGCT	180
GTCAAGAATT TTTATC	TTGA CTCTCTGAG	T TTTCTATTTT	ATATGACGCA AGTAAGAATT	240
TAATAATAAA GTGGGT			TGG TTA GTG CTC TCT	291
	Met Lys Ser	Gln Phe Ser	Trp Leu Val Leu Ser	
	1	5	10	

TCG Ser	ACA Thr	TTG Leu	GCA Ala 15	TGT Cys	TTT Phe	ACT Thr	AGT Ser	TGT Cys 20	TCC Ser	ACT Thr	GTT Val	TTT Phe	GCT Ala 25	GCA Ala	ACT Thr	339
GCT Ala	GAA Glu	AAT Asn 30	ATA Ile	GGC Gly	CCC Pro	TCT Ser	GAT Asp 35	AGC Ser	TTT Phe	GAC Asp	GGA Gly	AGT Ser 40	ACT Thr	AAC Asn	ACA Thr	387
GGC Gly	ACC Thr 45	TAT Tyr	ACT Thr	CCT Pro	AAA Lys	AAT Asn 50	ACG Thr	ACT Thr	ACT Thr	GGA Gly	ATA Ile 55	GAC Asp	TAT Tyr	ACT Thr	CTG Leu	435
ACA Thr 60	GGA Gly	GAT Asp	ATA Ile	ACT Thr	CTG Leu 65	CAA Gln	AAC Asn	CTT Leu	GGG Gly	GAT Asp 70	TCG Ser	GCA Ala	GCT Ala	TTA Leu	ACG Thr 75	483
AAG Lys	GGT Gly	TGT Cys	TTT Phe	TCT Ser 80	GAC Asp	ACT Thr	ACG Thr	GAA Glu	TCT Ser 85	TTA Leu	AGC Ser	TTT Phe	GCC Ala	GGT Gly 90	AAG Lys	531
GGG Gly	TAC Tyr	TCA Ser	CTT Leu 95	TCT Ser	TTT Phe	TTA Leu	AAT Asn	ATT Ile 100	AAG Lys	TCT Ser	AGT Ser	GCT Ala	GAA Glu 105	GGC Gly	GCA Ala	579
GCA Ala	CTT Leu	TCT Ser 110	GTT Val	ACA Thr	ACT Thr	GAT Asp	AAA Lys 115	AAT Asn	CTG Leu	TCG Ser	CTA Leu	ACA Thr 120	GGA Gly	TTT Phe	TCG Ser	627
AGT Ser	CTT Leu 125	ACT Thr	TTC Phe	TTA Leu	GCG Ala	GCC Ala 130	CCA Pro	TCA Ser	TCG Ser	GTA Val	ATC Ile 135	ACA Thr	ACC Thr	CCC Pro	TCA Ser	675
GGA Gly 140	AAA Lys	GGT Gly	GCA Ala	GTT Val	AAA Lys 145	TGT Cys	GGA Gly	GGG Gly	GAT Asp	CTT Leu 150	ACA Thr	TTT Phe	GAT Asp	AAC Asn	AAT Asn 155	723
GGA Gly	ACT Thr	ATT Ile	TTA Leu	TTT Phe 160	AAA Lys	CAA Gln	GAT Asp	TAC Tyr	TGT Cys 165	GAG Glu	GAA Glu	AAT Asn	GGC Gly	GGA Gly 170	GCC Ala	771
ATT Ile	TCT Ser	ACC Thr	AAG Lys 175	AAT Asn	CTT Leu	TCT Ser	TTG Leu	AAA Lys 180	AAC Asn	AGC Ser	ACG Thr	GGA Gly	TCG Ser 185	ATT Ile	TCT Ser	819
TTT Phe	GAA Glu	GGG Gly 190	Asn	AAA Lys	TCG Ser	AGC Ser	GCA Ala 195	ACA Thr	GGG Gly	AAA Lys	AAA Lys	GGT Gly 200	GGG Gly	GCT Ala	ATT Ile	867
TG1 Cys	GCT Ala 205	Thr	GGT Gly	ACT Thr	GTA Val	GAT Asp 210	ATT	ACA Thr	AAT Asn	AAT Asn	ACG Thr 215	GCT Ala	CCT Pro	ACC Thr	CTC Leu	915
TT(Phe 22(TCG Ser	AAC Asn	AAT Asn	ATT Ile	GCT Ala 225	Glu	GCT Ala	GCA Ala	GGT Gly	GGA Gly 230	Ala	ATA Ile	AAT Asn	AGC Ser	ACA Thr 235	963
GG	AAC	TGT	: ACA	ATT	ACA	GGG	TAA	' ACG	TCT	CTT	GTA	TTT	TCT	GAA	AAT	1011

										, ,						
Gly	Asn	Cys	Thr	Ile 240	Thr	Gly	Asn	Thr	Ser 245	Leu	Val	Phe	Ser	Glu 250	Asn	
AGT Ser	GTG Val	ACA Thr	GCG Ala 255	ACC Thr	GCA Ala	GGA Gly	AAT Asn	GGA Gly 260	GGA Gly	GCT Ala	CTT Leu	TCT Ser	GGA Gly 265	GAT Asp	GCC Ala	1059
GAT Asp	GTT Val	ACC Thr 270	ATA Ile	TCT Ser	GGG Gly	AAT Asn	CAG Gln 275	AGT Ser	GTA Val	ACT Thr	TTC Phe	TCA Ser 280	GGA Gly	AAC Asn	CAA Gln	1107
Ala	Val 285	Ala	Asn	Gly	Gly	Ala 290	Ile	Tyr	Ala	Lys	Lys 295	Leu	Thr	CTG Leu	Ala	1155
TCC Ser 300	GGG Gly	GGG Gly	GGG Gly	GGG Gly	GGT Gly 305	ATC Ile	TCC Ser	TTT Phe	TCT Ser	AAC Asn 310	AAT Asn	ATA Ile	GTC Val	CAA Gln	GGT Gly 315	1203
ACC Thr	ACT Thr	GCA Ala	GGT Gly	AAT Asn 320	GGT Gly	GGA Gly	GCC Ala	ATT Ile	TCT Ser 325	ATA Ile	CTG Leu	GCA Ala	GCT Ala	GGA Gly 330	GAG Glu	1251
TGT Cys	AGT Ser	CTT Leu	TCA Ser 335	GCA Ala	GAA Glu	GCA Ala	GGG Gly	GAC Asp 340	ATT Ile	ACC Thr	TTC Phe	AAT Asn	GGG Gly 345	AAT Asn	GCC Ala	1299
ATT Ile	GTT Val	GCA Ala 350	ACT Thr	ACA Thr	CCA Pro	CAA Gln	ACT Thr 355	ACA Thr	AAA Lys	AGA Arg	AAT Asn	TCT Ser 360	ATT Ile	GAC Asp	ATA Ile	1347
GGA Gly	TCT Ser 365	ACT Thr	GCA Ala	AAG Lys	ATC Ile	ACG Thr 370	AAT Asn	TTA Leu	CGT Arg	GCA Ala	ATA Ile 375	TCT Ser	GGG Gly	CAT His	AGC Ser	1395
ATC Ile 380	TTT Phe	TTC Phe	TAC Tyr	GAT Asp	CCG Pro 385	ATT Ile	ACT Thr	GCT Ala	AAT Asn	ACG Thr 390	GCT Ala	GCG Ala	GAT Asp	TCT Ser	ACA Thr 395	1443
GAT Asp	ACT Thr	TTA Leu	AÁT Asn	CTC Leu 400	AAT Asn	AAG Lys	GCT Ala	GAT Asp	GCA Ala 405	GGT Gly	AAT Asn	AGT Ser	ACA Thr	GAT Asp 410	TAT Tyr	1491
AGT Ser	GGG Gly	TCG Ser	ATT Ile 415	GTT Val	TTT Phe	TCT Ser	GGT Gly	GAA Glu 420	AAG Lys	CTC Leu	TCT Ser	GAA Glu	GAT Asp 425	GAA Glu	GCA Ala	1539
AAA Lys	GTT Val	GCA Ala 430	GAC Asp	AAC Asn	CTC Leu	ACT Thr	TCT Ser 435	ACG Thr	CTG Leu	AAG Lys	CAG Gln	CCT Pro 440	GTA Val	ACT Thr	CTA Leu	1587
ACT Thr	GCA Ala 445	GGA Gly	AAT Asn	TTA Leu	GTA Val	CTT Leu 450	AAA Lys	CGT Arg	GGT Gly	GTC Val	ACT Thr 455	CTC Leu	GAT Asp	ACG Thr	AAA Lys	1635
GGC Gly	TTT Phe	ACT Thr	CAG Gln	ACC Thr	GCG Ala	GGT Gly	TCC Ser	TCT Ser	GTT Val	ATT Ile	ATG Met	GAT Asp	GCG Ala	GGC Gly	ACA Thr	1683

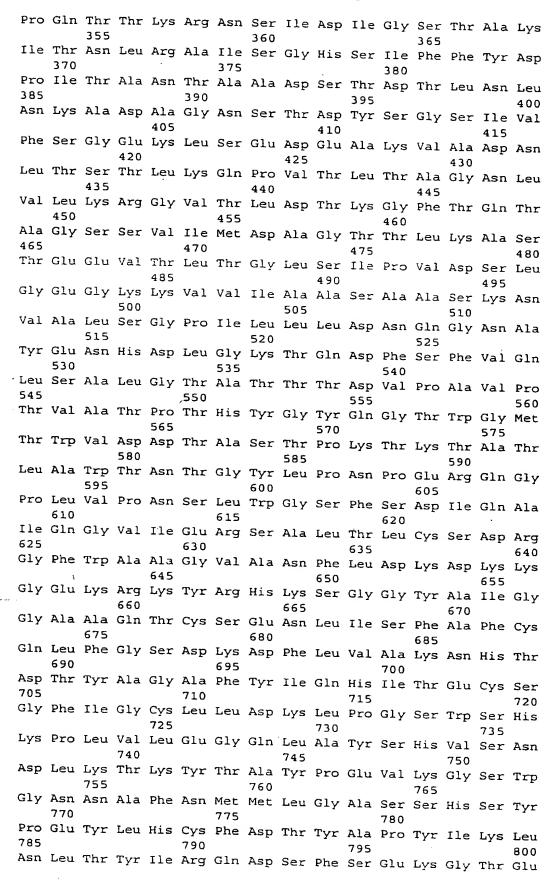
460	465	470	475
ACG TTA AAA GCA AGT Thr Leu Lys Ala Ser 480	ACA GAG GAG GTC Thr Glu Glu Val	ACT TTA ACA GGT CTT Thr Leu Thr Gly Leu 485	TCC ATT 1731 Ser Ile 490
CCT GTA GAC TCT TTA Pro Val Asp Ser Leu 495	GGC GAG GGT AAG Gly Glu Gly Lys 500	AAA GTT GTA ATT GCT Lys Val Val Ile Ala 505	GCT TCT 1779 Ala Ser
GCA GCA AGT AAA AAT Ala Ala Ser Lys Asn 510	GTA GCC CTT AGT Val Ala Leu Ser 515	GGT CCG ATT CTT CTT Gly Pro Ile Leu Leu 520	TTG GAT 1827 Leu Asp
AAC CAA GGG AAT GCT Asn Gln Gly Asn Ala 525	TAT GAA AAT CAC Tyr Glu Asn His 530	GAC TTA GGA AAA ACT Asp Leu Gly Lys Thr 535	CAA GAC 1875 Gln Asp
TTT TCA TTT GTG CAG Phe Ser Phe Val Gln 540	CTC TCT GCT CTG Leu Ser Ala Leu 545	GGT ACT GCA ACA ACT Gly Thr Ala Thr Thr 550	ACA GAT 1923 Thr Asp 555
GTT CCA GCG GTT CCT Val Pro Ala Val Pro 560	ACA GTA GCA ACT Thr Val Ala Thr	CCT ACG CAC TAT GGG Pro Thr His Tyr Gly 565	TAT CAA 1971 Tyr Gln 570
GGT ACT TGG GGA ATG Gly Thr Trp Gly Met 575	ACT TGG GTT GAT Thr Trp Val Asp 580	GAT ACC GCA AGC ACT Asp Thr Ala Ser Thr 585	CCA AAG 2019 Pro Lys
ACT AAG ACA GCG ACA Thr Lys Thr Ala Thr 590	TTA GCT TGG ACC Leu Ala Trp Thr 595	AAT ACA GGC TAC CTT Asn Thr Gly Tyr Leu 600	CCG AAT 2067 Pro Asn
CCT GAG CGT CAA GGA Pro Glu Arg Gln Gly 605	CCT TTA GTT CCT Pro Leu Val Pro 610	AAT AGC CTT TGG GGA Asn Ser Leu Trp Gly 615	TCT TTT 2115 Ser Phe
TCA GAC ATC CAA GCG Ser Asp Ile Gin Ala 620	ATT CAA GGT GTC Ile Gln Gly Val 625	ATA GAG AGA AGT GCT Ile Glu Arg Ser Ala 630	TTG ACT 2163 Leu Thr 635
CTT TGT TCA GAT CGA Leu Cys Ser Asp Arg 640	GGC TTC TGG GCT Gly Phe Trp Ala	GCG GGA GTC GCC AAT Ala Gly Val Ala Asn 645	TTC TTA 2211 Phe Leu 650
GAT AAA GAT AAG AAA Asp Lys Asp Lys Lys 655	GGG GAA AAA CGC Gly Glu Lys Arg 660	AAA TAC CGT CAT AAA Lys Tyr Arg His Lys 665	TCT GGT 2259 Ser Gly
GGA TAT GCT ATC GGA Gly Tyr Ala Ile Gly 670	GGT GCA GCG CAA Gly Ala Ala Gln 675	ACT TGT TCT GAA AAC Thr Cys Ser Glu Asn 680	TTA ATT 2307 Leu Ile
AGC TTT GCC TTT TGC Ser Phe Ala Phe Cys 685	CAA CTC TTT GGT Gln Leu Phe Gly 690	AGC GAT AAA GAT TTC Ser Asp Lys Asp Phe 695	TTA GTC 2355 Leu Val

GCT Ala 700	AAA Lys	AAT Asn	CAT His	ACT Thr	GAT Asp 705	ACC Thr	TAT Tyr	GCA Ala	GGA Gly	GCC Ala 710	TTC Phe	TAT Tyr	ATC Ile	CAA Gln	CAC His 715	2403
ATT Ile	ACA Thr	GAA Glu	TGT Cys	AGT Ser 720	GGG Gly	TTC Phe	ATA Ile	GGT Gly	TGT Cys 725	CTC Leu	TTA Leu	GAT Asp	AAA Lys	CTT Leu 730	CCT Pro	2451
GGC Gly	TCT Ser	TGG Trp	AGT Ser 735	CAT His	AAA Lys	CCC Pro	CTC Leu	GTT Val 740	TTA Leu	GAA Glu	GGG Gly	CAG Gln	CTC Leu 745	GCT Ala	TAT Tyr	2499
AGC Ser	CAC His	GTC Val 750	AGT Ser	AAT Asn	GAT Asp	CTG Leu	AAG Lys 755	ACA Thr	AAG Lys	TAT Tyr	ACT Thr	GCG Ala 760	TAT Tyr	CCT Pro	GAG Glu	2547
Val	Lys 765	Gly	Ser	Trp	GGG Gly	Asn 770	Asn	Ala	Phe	Asn	Met 775	Met	Leu	Gly	Ala	2595
Ser 780	Ser	His	Ser	Tyr	CCT Pro 785	Glu	Tyr	Leu	His	Cys 790	Phe	Asp	Thr	Tyr	Ala 795	2643
Pro	Tyr	Ile	Lys	Leu 800	AAT Asn	Leu	Thr	Tyr	Ile 805	Arg	Gln	Asp	Ser	Phe 810	Ser	2691
Glu	Lys	Gly	Thr 815	Glu	GGA Gly	Arg	Ser	Phe 820	Asp	Asp	Ser	Asn	Leu 825	Phe	Asn	2739
Leu	Ser	Leu 830	Pro	Ile	GGG Gly	Val	Lys 835	Phe	Glu	Ļys	Phe	Ser 840	Asp	Cys	Asn	2787
Asp	Phe 845	Ser	Tyr	Asp	CTG Leu	Thr 850	Leu	Ser	Tyr	Val	Pro 855	Asp	Leu	Ile	Arg	2835
Asn 860	Asp	Pro	Lys	Cys	ACT Thr 865	Thr	Ala	Leu	Val	Ile 870	Ser	Gly	Ala	Ser	Trp 875	2883
Glu	Thr	Tyr	Ala	880	AAC Asn	Leu	Ala	Arg	Gln 885	Ala	Leu	Gln	Val	Arg 890	Ala	2931
Gly	Ser	His	Tyr 895	Ala	TTC Phe	Ser	CCT Pro	ATG Met 900	TTT Phe	GAA Glu	GTG Val	CTC Leu	GGC Gly 905	CAG Gln	TTT Phe	2979 -
					GGA Gly											3000

(2) INFORMATION FOR SEQ ID NO:26:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 914 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

+	Lys			2					10					15	
	Thr		20					25					3.0	Ile	
	Ser	22					40					45			
	Asn 50					55					60				
0.5	Gln				70					75					9.0
	Thr			0.5					90					95	
	Leu		TOO					105					110		
	Asp	113					120					125			
	Ala 130					135					140				
747	Cys				T20					155					160
	Gln			T 0 2					170	•				175	
	Ser		T80					185					190		
	Ser	TEE					200					205			
	Asp 210					215					220				
225	Glu				230					235					240
	Gly			245					250					255	
	Gly		200					265					270		
	Asn	215					280					285			
	Ala 290					295					300				
202	Ile				.3 LU					२15					2 2 0
	Gly			323					330					225	
GIU	Ala	σтλ	340	iie	Thr	Phe	Asn	Gly 345	Asn	Ala	Ile	Val	Ala 350	Thr	Thr



_				805					810					815	
			820					825					830	Pro	
		835					840					845		Tyr	
	850					855					860			Lys	_
Thr 865	Thr	Ala	Leu	Val	Ile 870	Ser	Gly	Ala	Ser	Trp 875	Glu	Thr	Tyr	Ala	Asn 880
Asn	Leu	Ala	Arg	Gln 885	Ala	Leu	Gln	Val	Arg 890	Ala	Gly	Ser	His	Tyr 895	Ala
Phe	Ser	Pro	Met 900	Phe	Glu	Val	Leu	Gly 905	Gln	Phe	Val	Phe	Glu 910	Val	Arg
Gly	Ser												210		

(2) INFORMATION FOR SEQ ID NO:27:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1200 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: Coding Sequence
- (B) LOCATION: 1...1200
- (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

GAT Asp 1	Pro	AAA Lys	AAT Asn	AAA Lys 5	GAG Glu	TAC Tyr	ACA Thr	GGG Gly	ACC Thr 10	ATA Ile	CTC Leu	TTT Phe	TCT Ser	GGA Gly 15	GAA Glu	48
AAG Lys	AGT Ser	CTA Leu	GCA Ala 20	AAC Asn	GAT Asp	CCT Pro	AGG Arg	GAT Asp 25	TTT Phe	AAA Lys	TCT Ser	ACA Thr	ATC Ile 30	CCT Pro	CAG Gln	96
AAC Asn	GTC Val	AAC Asn 35	CTG Leu	TCT Ser	GCA Ala	GGA Gly	TAC Tyr 40	TTA Leu	GTT Val	ATT Ile	AAA Lys	GAG Glu 45	GGG Gly	GCC Ala	GAA Glu	144
GTC Val	ACA Thr 50	GTT Val	TCA Ser	AAA Lys	TTC Phe	ACG Thr 55	CAG Gln	TCT Ser	CCA Pro	GGA Gly	TCG Ser 60	CAT His	TTA Leu	GTT Val	TTA Leu	192
GAT Asp 65	TTA Leu	GGA Gly	ACC Thr	AAA Lys	CTG Leu 70	ATA Ile	GCC Ala	TCT Ser	AAG Lys	GAA Glu 75	GAC Asp	ATT Ile	GCC Ala	ATC Ile	ACA Thr 80	240
GGC Gly	CTC Leu	GCG Ala	ATA Ile	GAT Asp 85	ATA Ile	GAT Asp	AGC Ser	TTA Leu	AGC Ser 90	TCA Ser	TCC Ser	TCA Ser	ACA Thr	GCA Ala 95	GCT Ala	288

GTT Val	ATT Ile	AAA Lys	GCA Ala 100	AAC Asn	ACC Thr	GCA Ala	AAT Asn	AAA Lys 105	CAG Gln	ATA Ile	TCC Ser	GTG Val	ACG Thr 110	GAC Asp	TCT Ser	336
ATA Ile	GAA Glu	CTT Leu 115	ATC Ile	TCG Ser	CCT Pro	ACT Thr	GGC Gly 120	AAT Asn	GCC Ala	TAT Tyr	GAA Glu	GAT Asp 125	CTC Leu	AGA Arg	ATG Met	384
AGA Arg	AAT Asn 130	TCA Ser	CAG Gln	ACG Thr	TTC Phe	CCT Pro 135	CTG Leu	CTC Leu	TCT Ser	TTA Leu	GAG Glu 140	CCT Pro	GGA Gly	GCC Ala	GGG Gly	432
GGT Gly 145	AGT Ser	GTG Val	ACT Thr	GTA Val	ACT Thr 150	GCT Ala	GGA Gly	GAT Asp	TTC Phe	CTA Leu 155	CCG Pro	GTA Val	AGT Ser	CCC Pro	CAT His 160	480
TAT Tyr	GGT Gly	TTT Phe	CAA Gln	GGC Gly 165	AAT Asn	TGG Trp	AAA Lys	TTA Leu	GCT Ala 170	TGG Trp	ACA Thr	GGA Gly	ACT Thr	GGA Gly 175	AAC Asn	528
AAA Lys	GTT Val	GGA Gly	GAA Glu 180	TTC Phe	TTC Phe	TGG Trp	GAT Asp	AAA Lys 185	ATA Ile	AAT Asn	TAT Tyr	AAG Lys	CCT Pro 190	AGA Arg	CCT Pro	576
GAA Glu	AAA Lys	GAA Glu 195	GGA Gly	AAT Asn	TTA Leu	GTT Val	CCT Pro 200	AAT Asn	ATC Ile	TTG Leu	TGG Trp	GGG Gly 205	AAT Asn	GCT Ala	GTA Val	624
AAT Asn	GTC Val 210	AGA Arg	TCC Ser	TTA Leu	ATG Met	CAG Gln 215	GTT Val	CAA Gln	GAG Glu	ACC Thr	CAT His 220	GCA Ala	TCG Ser	AGC Ser	TTA Leu	672
CAG Gln 225	ACA Thr	GAT Asp	CGA Arg	GGG Gly	CTG Leu 230	TGG Trp	ATC Ile	GAT Asp	GGA Gly	ATT Ile 235	GGG Gly	AAT Asn	TTC Phe	TTC Phe	CAT His 240	720
GTA Val	TCT Ser	GCC Ala	TCC Ser	GAA Glu 245	GAC Asp	AAT Asn	ATA Ile	AGG Arg	TAC Tyr 250	CGT Arg	CAT His	AAC Asn	AGC Ser	GGT Gly 255	GGA Gly	768
TAT Tyr	GTT Val	CTA Leu	TCT Ser 260	GTA Val	AAT Asn	AAT Asn	GAG Glu	ATC Ile 265	ACA Thr	CCT Pro	AAG Lys	CAC His	TAT Tyr 270	ACT Thr	TCG Ser	816
ATG Met	GCA Ala	TTT Phe 275	TCC Ser	CAA Gln	CTC Leu	TTT Phe	AGT Ser 280	AGA Arg	GAC Asp	AAA Lys	GAC Asp	TAT Tyr 285	GCG Ala	GTT Val	TCC Ser	864
AAC Asn	AAC Asn 290	GAA Glu	TAC Tyr	AGA Arg	ATG Met	TAT Tyr 295	TTA Leu	GGA Gly	TCG Ser	TAT Tyr	CTC Leu 300	TAT Tyr	CAA Gln	TAT Tyr	ACA Thr	912
ACC Thr 305	TCC Ser	CTA Leu	GGG Gly	AAT Asn	ATT Ile 310	TTC Phe	CGT Arg	TAT Tyr	GCT Ala	TCG Ser 315	CGT Arg	AAC Asn	CCT Pro	AAT Asn	GTA Val 320	960
AAC	GTC	GGG	ATT	CTC	TCA	AGA	AGG	TTT	CTT	CAA	AAT	CCT	CTT	ATG	ATT	1008

Asn	Val	Gly	Ile	Leu 325	Ser	Arg	Arg	Phe	Leu 330	Gln	Asn	Pro	Leu	Met 335	Ile	
TTT Phe	CAT His	TTT Phe	TTG Leu 340	TGT Cys	GCT Ala	TAT Tyr	GGT Gly	CAT His 345	GCC Ala	ACC Thr	AAT Asn	GAT Asp	ATG Met 350	AAA Lys	ACA Thr	1056
GAC Asp	TAC Tyr	GCA Ala 355	AAT Asn	TTC Phe	CCT Pro	ATG Met	GTG Val 360	AAA Lys	AAC Asn	AGC Ser	TGG Trp	AGA Arg 365	AAC Asn	AAT Asn	TGT Cys	1104
TGG Trp	GCT Ala 370	ATA Ile	AAA Lys	TGC Cys	GGA Gly	GGG Gly 375	AGC Ser	ATG Met	CCT Pro	CTA Leu	TTG Leu 380	GTA Val	TTT Phe	GAA Glu	AAC Asn	1152
GGA Gly 385	AAA Lys	CTT Leu	TTC Phe	CAA Gln	GGT Gly 390	GCC Ala	ATC Ile	CCA Pro	TTT Phe	ATG Met 395	AAA Lys	CTA Leu	CAA Gln	TTA Leu	GTT Val 400	1200

(2) INFORMATION FOR SEQ ID NO:28:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 400 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

	1			Asn	· 5					10					15	
				Ala 20					25					30		
			35	Leu				40					45			
		50		Ser			55					60				
6	5			Thr		70					75					8.0
				Ile	85					90					95	
				Ala 100					105					110	_	
			115	Ile				120					125	Leu		
A	rg	Asn 130	Ser	Gln	Thr	Phe	Pro 135	Leu	Leu	Ser	Leu	Glu 140	Pro	Gly	Ala	Gly
1	31y .45	Ser	Val	Thr	Val	Thr 150	Ala	Gly	Asp	Phe	Leu 155	Pro	Val	Ser	Pro	His 160
T	yr	Gly	Phe	Gln	Gly 165	Asn	Trp	Lys	Leu	Ala 170	Trp	Thr	Gly	Thr	Gly 175	Asn
I	ys	Val	Gly	Glu 180	Phe	Phe	Trp	Asp	Lys 185		Asn		Lys	Pro	Arg	Pro

Glu	Lys	Glu 195	Gly	Asn	Leu	Val	Pro 200	Asn	Ile	Leu	Trp		Asn	Ala	Val
7.00	17.7		C 0 x	T 0	N4	01 -						205			
ASII	vai	ALG	ser	Leu	Mec	Gln	vaı	Gin	Glu	Thr	His	Ala	Ser	Ser	Leu
	210	_				215					220				
Gln	Thr	Asp	Arg	Gly	Leu	Trp	Ile	Asp	Gly	Ile	Gly	Asn	Phe	Phe	His
225					230					235					240
Val	Ser	Ala	Ser	Glu	Asp	Asn	Ile	Arg	Tyr	Arq	His	Asn	Ser	Glv	Glv
				245				_	250	. 3		-		255	1
Tyr	Val	Leu	Ser	Val	Asn	Asn	Glu	Ile	Thr	Pro	Lvs	His	Tyr	Thr	Sar
			260					265			2,5		270	****	361
Met	Ala	Phe	Ser	Gln	Leu	Phe	Ser		Acn	Lace	7.55	Т~		17-3	C
		275					280	n. g	rap	пуз	ASD		Ala	vai	ser
Asn	Asn		Tyr	Ara	Met	Tyr		C1	C		.	285	~ 1	_	
	290		- 7 -	9	riec	295	Leu	GIA	ser	Tyr		Tyr	GIn	Tyr	Thr
Thr		T 011	C1	7	T1 -			_		_	300				
305	261	Leu	GIY	ASII	ile	Phe	Arg	Tyr	Ala		Arg	Asn	Pro	Asn	Val
	17 3	G1	- 1		310	_				315					320
Asn	vai	GLY	TIE	Leu	Ser	Arg	Arg	Phe	Leu	Gln	Asn	Pro	Leu	Met	Ile
				325					330					335	
Phe	His	Phe	Leu	Cys	Ala	Tyr	Gly	His	Ala	Thr	Asn	Asp	Met	Lys	Thr
			340					345					350		
Asp	Tyr	Ala	Asn	Phe	Pro	Met	Val	Lys	Asn	Ser	Trp	Arq	Asn	Asn	Cvs
		355					360					365			
Trp	Ala	Ile	Lys	Cys	Gly	Gly	Ser	Met	Pro	Leu	Leu	Val	Phe	Glu	Acn
	370				_	375					380		• • • •	Olu	7311
Gly	Lys	Leu	Phe	Gln	Glv	Ala	Ile	Pro	Phe	Met	Lve	Len	Cln.	T 011	W-1
385	-				390		_ ~ ~	- 2 0		395	273	Deu	GIII	neu	
										223					400

(2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1830 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: Coding Sequence
 - (B) LOCATION: 1...1830
 - (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Asp 1	Leu	Thr	Leu	GGG Gly 5	AGT Ser	Arg	GAC Asp	AGT Ser	TAT Tyr 10	AAT Asn	GGT Gly	GAT Asp	ACA Thr	AGC Ser 15	ACC Thr	48
ACA Thr	GAA Glu	TTT Phe	ACT Thr 20	CCT Pro	AAA Lys	GCG Ala	GCA Ala	ACT Thr 25	TCT Ser	GAT Asp	GCT Ala	AGT Ser	GGC Gly 30	ACG Thr	ACC Thr	96
TAT Tyr	ATT Ile	CTC Leu 35	GAT Asp	GGG Gly	GAT Asp	GTC Val	TCG Ser 40	ATA Ile	AGC Ser	CAA Gln	GCA Ala	GGG Gly 45	AAA Lys	CAA Gln	ACG Thr	144

WO 98/58953 PCT/DK98/00266

AGC Ser	TTA Leu 50	ACC Thr	ACA Thr	AGT Ser	TGT Cys	TTT Phe 55	TCT Ser	AAC Asn	ACT Thr	GCA Ala	GGA Gly 60	AAT Asn	CTT Leu	ACC Thr	TTC Phe	192
TTA Leu 65	GGG Gly	AAC Asn	GGA Gly	TTT Phe	TCT Ser 70	CTT Leu	CAT His	TTT Phe	GAC Asp	AAT Asn 75	ATT Ile	ATT Ile	TCG Ser	TCT Ser	ACT Thr 80	240
GTT Val	GCA Ala	GGT Gly	GTT Val	GTT Val 85	GTT Val	AGC Ser	AAT Asn	ACA Thr	GCA Ala 90	GCT Ala	TCT Ser	GGG Gly	ATT Ile	ACG Thr 95	AAA Lys	288
TTC Phe	TCA Ser	GGA Gly	TTT Phe 100	TCA Ser	ACT Thr	CTT Leu	CGG Arg	ATG Met 105	CTT Leu	GCA Ala	GCT Ala	CCT Pro	AGG Arg 110	ACC Thr	ACA Thr	336
GGT Gly	AAA Lys	GGA Gly 115	GCC Ala	ATT Ile	AAA Lys	ATT Ile	ACC Thr 120	GAT Asp	GGT Gly	CTG Leu	GTG Val	TTT Phe 125	GAG Glu	AGT Ser	ATA Ile	384
GGG Gly	AAT Asn 130	CTT Leu	GAT Asp	CCG Pro	ATT Ile	ACT Thr 135	GTA Val	ACA Thr	GGA Gly	TCG Ser	ACA Thr 140	TCT Ser	GTT Val	GCT Ala	GAT Asp	432
GCT Ala 145	CTC Leu	AAT Asn	ATT Ile	AAT Asn	AGC Ser 150	CCT Pro	GAT Asp	ACT Thr	GGA Gly	GAT Asp 155	AAC Asn	AAA Lys	GAG Glu	TAT Tyr	ACG Thr 160	480
GGA Gly	ACC Thr	ATA Ile	GTC Val	TTT Phe 165	TCT Ser	GGA Gly	GAG Glu	AAG Lys	CTC Leu 170	ACG Thr	GAG Glu	GCA Ala	GAA Glu	GCT Ala 175	AAA Lys	528
GAT Asp	GAG Glu	AAG Lys	AAC Asn 180	CGC Arg	ACT Thr	TCT Ser	AAA Lys	TTA Leu 185	CTT Leu	CAA Gln	AAT Asn	GTT Val	GCT Ala 190	TTT Phe	AAA Lys	576
AAT Asn	GGG Gly	ACT Thr 195	GTA Val	GTT Val	TTA Leu	AAA Lys	GGT Gly 200	GAT Asp	GTC Val	GTT Val	TTA Leu	AGT Ser 205	GCG Ala	AAC Asn	GGT Gly	624
TTC Phe	TCT Ser 210	CAG Gln	GAT Asp	GCA Ala	AAC Asn	TCT Ser 215	AAG Lys	TTG Leu	ATT Ile	ATG Met	GAT Asp 220	TTA Leu	GGG Gly	ACG Thr	TCG Ser	672
TTG Leu 225	GTT Val	GCA Ala	AAC Asn	ACC Thr	GAA Glu 230	AGT Ser	ATC Ile	GAG Glu	TTA Leu	ACG Thr 235	Asn	TTG Leu	GAA Glu	ATT Ile	AAT Asn 240	720
ATA Ile	GAC Asp	TCT Ser	CTC Leu	AGG Arg 245	AAC Asn	GGG Gly	AAA Lys	AAG Lys	ATA Ile 250	AAA Lys	CTC Leu	AGT Ser	GCT Ala	GCC Ala 255	ACA Thr	768
GCT Ala	CAG Gln	AAA Lys	GAT Asp 260	Ile	CGT Arg	ATA Ile	GAT Asp	CGT Arg 265	Pro	GTT Val	GTA Val	CTG Leu	GCA Ala 270	ATT Ile	AGC Ser	816
GAT	' GAG	AGI	TTT	TAT	CAA	AAT	GGC	TTT	TTG	AAT	' GAG	GAC		TCC	TAT	864

									,							
Asp	Glu	Ser 275	Phe	Tyr	Gln	Asn	Gly 280	Phe	Leu	Asn	Glu	Asp 285	His	Ser	Tyr	
GAT Asp	GGG Gly 290	ATT Ile	CTT Leu	GAG Glu	TTA Leu	GAT Asp 295	GCT Ala	GGG Gly	AAA Lys	GAC Asp	ATC Ile 300	GTG Val	ATT Ile	TCT Ser	GCA Ala	912
GAT Asp 305	TCT Ser	CGC Arg	AGT Ser	ATA Ile	GAT Asp 310	GCT Ala	GTA Val	CAA Gln	TCT Ser	CCG Pro 315	TAT Tyr	GGC Gly	TAT Tyr	CAG Gln	GGA Gly 320	960
Lys	Trp	ACG Thr	Ile	Asn 325	Trp	Ser	Thr	Asp	Asp 330	Lys	Lys	Ala	Thr	Val 335	Ser	1008
TGG Trp	GCG Ala	AAG Lys	CAG Gln 340	AGT Ser	TTT Phe	AAT Asn	CCC Pro	ACT Thr 345	GCT Ala	GAG Glu	CAG Gln	GAG Glu	GCT Ala 350	CCG Pro	TTA Leu	1056
GTT Val	CCT Pro	AAT Asn 355	CTT Leu	CTT Leu	TGG Trp	GGT Gly	TCT Ser 360	TTT Phe	ATA Ile	GAT Asp	GTT Val	CGT Arg 365	TCC Ser	TTC Phe	CAG Gln	1104
AAT Asn	TTT Phe 370	ATA Ile	GAG Glu	CTA Leu	GGT Gly	ACT Thr 375	GAA Glu	GGT Gly	GCT Ala	CCT Pro	TAC Tyr 380	GAA Glu	AAG Lys	AGA Arg	TTT Phe	1152
TGG Trp 385	GTT Val	GCA Ala	GGC Gly	ATT Ile	TCC Ser 390	TAA Asn	GTT Val	TTG Leu	CAT His	AGG Arg 395	AGC Ser	GGT Gly	CGT Arg	GAA Glu	AAT Asn 400	1200
CAA Gln	AGG Arg	AAA Lys	TTC Phe	CGT Arg 405	CAT His	GTG Val	AGT Ser	GGA Gly	GGT Gly 410	GCT Ala	GTA Val	GTA Val	GGT Gly	GCT Ala 415	AGC Ser	1248
ACG Thr	AGG Arg	ATG Met	CCG Pro 420	GGT Gly	GGT Gly	GAT Asp	ACC Thr	TTG Leu 425	TCT Ser	CTG Leu	GGT Gly	TTT Phe	GCT Ala 430	CAG Gln	CTC Leu	1296
TTT Phe	GCG Ala	CGT Arg 435	GAC Asp	AAA Lys	GAC Asp	TAC Tyr	TTT Phe 440	ATG Met	AAT Asn	ACC Thr	AAT Asn	TTC Phe 445	GCA Ala	AAG Lys	ACC Thr	1344
TAC Tyr	GCA Ala 450	GGA Gly	TCT Ser	TTA Leu	CGT Arg	TTG Leu 455	CAG Gln	CAC	GAT Asp	GCT Ala	TCC Ser 460	CTA Leu	TAC Tyr	TCT Ser	GTG Val	1392
GTG Val 465	AGT Ser	ATC Ile	CTT Leu	TTA Leu	GGA Gly 470	GAG Glu	GGA Gly	GGA Gly	CTC Leu	CGC Arg 475	GAG Glu	ATC Ile	CTG Leu	TTG Leu	CCT Pro 480	1440
TAT Tyr	GTT Val	TCC Ser	AAT Asn	ACT Thr 485	CTG Leu	CCG Pro	TGC Cys	TCT Ser	TTC Phe 490	TAT	GGG Gly	CAG Gln	CTT Leu	AGC Ser 495	TAC Tyr	1488
GGC Gly	CAT His	ACG Thr	GAT Asp	CAT His	CGC Arg	ATG Met	AAG Lys	ACC Thr	GAG Glu	TCT Ser	CTA Leu	CCC Pro	CCC Pro	CCC Pro	CCC Pro	. 1536

86

			500					505					510			
CCG Pro	ACG Thr	CTC Leu 515	TCG Ser	ACG Thr	GAT Asp	CAT His	ACT Thr 520	TCT Ser	TGG Trp	GGA Gly	GGA Gly	TAT Tyr 525	GTC Val	TGG Trp	GCT Ala	1.584
GGA Gly	GAG Glu 530	CTG Leu	GGA Gly	ACT Thr	CGA Arg	GTT Val 535	GCT Ala	GTT Val	GAA Glu	AAT Asn	ACC Thr 540	AGC Ser	GGC Gly	AGA Arg	GGA Gly	1632
TTT Phe 545	TTC Phe	CGA Arg	GAG Glu	TAC Tyr	ACT Thr 550	CCA Pro	TTT Phe	GTA Val	AAA Lys	GTC Val 555	CAA Gln	GCT Ala	GTT Val	TAC Tyr	TCG Ser 560	1680
CGC Arg	CAA Gln	GAT Asp	AGC Ser	TTT Phe 565	GTT Val	GAA Glu	CTA Leu	GGA Gly	GCT Ala 570	ATC Ile	AGT Ser	CGT Arg	GAT Asp	TTT Phe 575	AGT Ser	1728
GAT Asp	TCG Ser	CAT His	CTT Leu 580	TAT Tyr	AAC Asn	CTT Leu	GCG Ala	ATT Ile 585	CCT Pro	CTT Leu	GGA Gly	ATC Ile	AAG Lys 590	TTA Leu	GAG Glu	1776
AAA Lys	CGG Arg	TTT Phe 595	GCA Ala	GAG Glu	CAA Gln	TAT Tyr	TAT Tyr 600	CAT His	GTT Val	GTT Val	GCG Ala	ATG Met 605	TAT Tyr	TCT Ser	CCA Pro	1824
	GTT Val 610															1830

(2) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 610 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

			100					105							
Glv	Lys	Glv		Ile	Lvs	Tle	Thr	105	Gly	Lau	1/01	Dha	110	0	~ 1
		115					120					125			
	Asn 130					135					140				_
Ala 145	Leu	Asn	Ile	Asn	Ser 150	Pro	Asp	Thr	Gly	Asp 155	Asn	Lys	Glu	Tyr	Thr 160
Gly	Thr	Ile	Val	Phe 165	Ser	Gly	Glu	Lys	Leu 170	Thr	Glu	Ala	Glu		Lys
Asp.	Glu	Lys	Asn 180		Thr	Ser	Lys	Leu 185		Gln	Asn	Val		175 Phe	Lys
Asn	Gly	Thr 195		Val	Leu	Lys	Gly		Val	Val	Leu		190 Ala	Asn	Gly
Phe	Ser 210		Asp	Ala	Asn	Ser 215	200 Lys	Leu	Ile	Met		205 Leu	Gly	Thr	Ser
Leu	Val	Ala	Asn	Thr	Glu		Ile	Glu	Leu		220 Asn	Leu	Glu	Ile	Asn
225 Ile	Ąsp	Ser	Leu	Arg	230 Asn	Gly	Lys	Lys	Ile	235 Lys	Leu	Ser	Ala	Ala	240 Thr
	Gln		Asp	245					250				•	255	
	Glu		260					265					270		
		275					280					285			
	Gly 290					295					300				
305	Ser				310					315					320
	Trp			325					330					335	
	Ala		340					345					350		
	Pro	355					360					365			
	Phe 370					375					380				
385	Val				390					395					400
	Arg			405					410					415	Ser
Thr	Arg	Met	Pro 420	Gly	Gly	Asp	Thr	Leu 425	Ser	Leu	Gly	Phe	Ala 430	Gln	Leu
Phe	Ala	Arg 435	Asp	Lys	Asp	Tyr	Phe 440		Asn	Thr	Asn	Phe 445	Ala	Lys	Thr
Tyr	Ala 450	Gly	Ser	Leu	Arg	Leu 455		His	Asp	Ala	Ser 460	Leu	Tyr	Ser	Val
Val 465	Ser	Ile	Leu	Leu	Gly 470		Gly	Gly	Leu	Arg 475	Glu	Ile	Leu	Leu	
	Val	Ser	Asn	Thr 485		Pro	Cys	Ser	Phe	Tyr	Gly	Gln	Leu		480 Tyr
Gly	His	Thr	Asp 500		Arg	Met	Lys	Thr	490 Glu	Ser	Leu	Pro	Pro	495 Pro	Pro
Pro	Thr	Leu		Thr	Asp	His	Thr	505 Ser	Trp	Gly	Gly	Tyr	510 Val	Trp	Ala
Gly	Glu	515 Leu	Gly	Thr	Arg	Val	520 Ala	Val	Glu	Asn		525 Ser	Gly	Arg	Gly
Phe	530 Phe				Thr	535					540				
545					550					555				-	560

Arg Gln Asp Ser Phe Val Glu Leu Gly Ala Ile Ser Arg Asp Phe Ser 575

Asp Ser His Leu Tyr Asn Leu Ala Ile Pro Leu Gly Ile Lys Leu Glu 580

Lys Arg Phe Ala Glu Gln Tyr Tyr His Val Val Ala Met Tyr Ser Pro 595

Asp Val 610

Claims

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subsequence thereof.

- 1. Species specific diagnostic test for identifying infection of a mammal, such as a human, with Chlamydia pneumoniae, said test comprising detecting in a patient or in a patient sample the presence of antibodies against one or more proteins from the outer membrane of Clamydia pneumoniae, said proteins being of a molecular weight of 100.3-89.6 kDa or of 56.1 kDa, or detecting the presence of nucleic acid fragments encoding said outer membrane proteins.
- Diagnostic test according to claim 1, wherein the outer membrane protein has the sequence as shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or in SEQ ID NO: 24, or a variant or subsequence thereof.
 - 3. Diagnostic test according to claim 1, wherein the nucleic acid fragment has the sequence shown in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or in SEQ ID NO: 23, or a variant or
 - 4. Diagnostic test according to claim 3 wherein detection of nucleic acid fragments is obtained by using nucleic acid amplification.
- 5. Diagnostic test according to claim 4, wherein detection of nucleic acid fragments is obtained by using polymerase chain reaction.
 - 6. A nucleic acid fragment derived from Chlamydia pneumoniae comprising the nucleotide sequence SEQ ID NO: 1, SEQ ID NO:
- 30 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23, or a variant or subsequent

of said nucleotide sequence which has a sequence homology of at least 50% with any of the sequences mentioned.

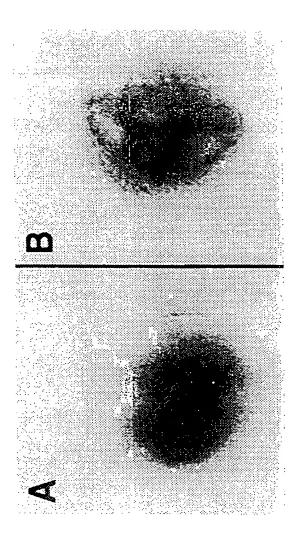
- 7. A protein derived from Chlamydia pneumoniae having the amino acid sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof having a sequence similarity of at least 50% and a similar biological function.
- 10 8. Polyclonal monospecific antibody against the protein with the sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof.
- 9. A diagnostic kit for the diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae, said kit comprising a protein with the amino acid sequence SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18,
 20 SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof.
- 10. A diagnostic kit for the diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae, said kit comprising antibodies against a protein with the amino acid sequence SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof.
- 11. A diagnostic kit for the diagnosis of infection of a mammal, such as a human, with *Chlamydia pneumoniae*, said kit comprising a nucleic acid fragment with the sequence SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO:

- 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23, or a variant or subsequence thereof.
- 12. A composition for immunizing a mammal, such as a human, against *Chlamydia pneumoniae*, said composition comprising a protein with the amino acid sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof.
- 13. Use of a protein with the sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof in diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae.
- 14. Use of the protein with the sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24 or a variant or subsequence thereof in an undenatured form, in diagnosis of infection of a mammal, such as a human, with Chlamydia pneumoniae.
- 15. Use of a protein with the sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 25 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof, for immunizing a mammal, such as a human, against Chlamydia pneumoniae.
- 16. Use of the protein with the sequence shown in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, or SEQ ID NO: 24, or a variant or subsequence thereof in an undenatured form, for

immunizing a mammal, such as a human, against Chlamydia pneumoniae.

17. Use of a nucleic acid fragment with the nucleotide sequence shown in SEQ ID NO: 1 SEQ ID NO: 3, SEQ ID NO: 5,

5 SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, or SEQ ID NO: 23, or a variant or subsequence of said nucleotide sequence which has a sequence homology of at least 50% with any of the sequences mentioned for immunizing a mammal, such as a human, against Chlamydia pneumoniae.



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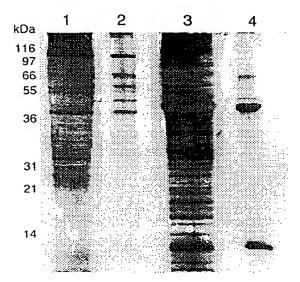


Fig. 2

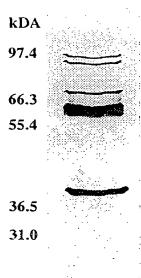


Fig. 3

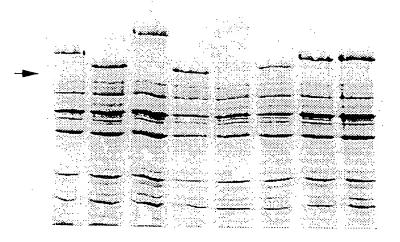


Fig. 4

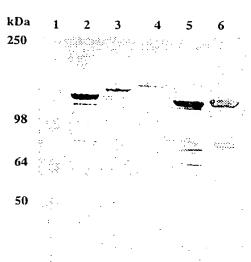


Fig. 5

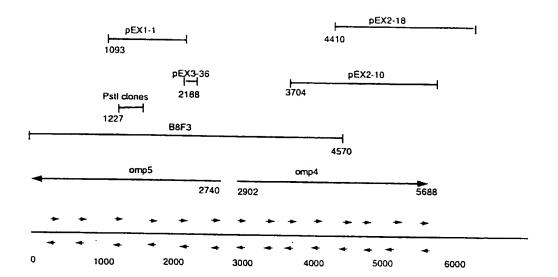


Fig. 6

C. pneumoniae omp4-15 gene clusters

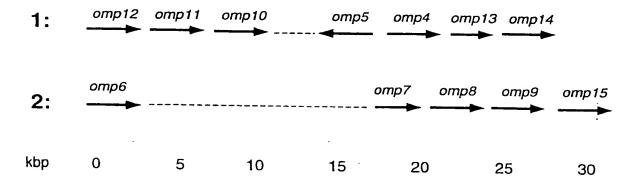


Fig. 7

| O O O O O O O E & O | SETEETSS | 国F ZXZXEZZOZZX 1 百 岁 日 日 文 日 日 日 二 日 王 00000000000 ことまままますの思られ **TAPUTUATU** | OOF SOOZ H A X O I E E O A S E E Z Z S E S H E S H E O 1 Z Z Q Q 1 Q Z Q Q Z Q | X f f A | H O f S H | IONZOZZOONZA I X O O O I I Z M F O A I · [O] [M [O O O] [D [O O O O O . 0 0 0 0 0 0 0 0 0 0 XEAHHHAASSA DOZONZHOEZO · HEFFFFFF I I 日内日日日日日日日日日日 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 · Z O Z O O O O Z · K Z · SS SS F F D E SS E SS SS ことららホメメリメスがら । २० ०० ०० ०००० LUCCOCCE · Ын<u>ы аааааа</u>н I NO NO NO NE NA D N > z f o z l o E o z > > ことれてひなりらけれらら 一中国山丸王田中田王V田 「臣丸口口臣臣中中すり〉 I H H H H H S N A H 1 1 1 D Z A E 1 Q E ·HUUUUUN 1112444144 1 KKSKKASHKES PARKIRARA I TA THE TE TE I QH HAAGERAGAAF 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 こなロとすなりじとほど HUXXXXXEZHZ ンプロエコマエマコマニュ 10000000000000 LCCDDDDDDCD · T > S & S E S Z S & F F I K E > H F O S I E I O I H Z Q Q Z E Q D D Z Z Z I H S S S S S S I O I A I Z Q M Z H X H Z M M A これの対しなってここ 一百工工日日日日日工工 1 2 2 1 1 2 1 2 2 2 1 1 エスススススの工工 | LI B M C L L L L D M C L L - 図ののののの回の HARDARAHHA OFFIREFERENCE · «HUUUUUUUU I H H S H S D I D S A H I FE H > Z S S F S H H · F S S S S S S I 上下 S F コエンととととととととこ 1 N N N N N N 1 N > O N L S C K H H H K H D K I тырны і навы HHEHHEHZDEE ではまけってんでなんこ | HOOOOAOHOOO PPODDAIADOPP I M Z J M Z Z Z F O Z X - PSSH用中SRCRR 101002106020 1 E 1 S A H 1 H A Z O S · NONEW W WE WHO OSSHSHFFF INFANONNNNIH XXXXXXXXXXX I H Z A I A F I F K H F ZZZZZZZZ - RXXXPXXX - XX omp12 omp8 omp5 omp11 omp10 omp15 omp15 omp15





Fig. 8B

224 228 228 222 220 222 172 161 235	266 261 261 262 262 272 181 260 168
12	2 G A I F T E A S V T I S N N A K V S F I D N K V T G A S S T T G D M S G G A I C
mo dwo dwo dwo dwo dwo dwo	omplomplomplomplomplomplomplomplomplompl





300 300 300 300 300 211 211 262	22348 3348 3348 3348 3348 3369 2568 2568
omp12	omp12
omplomplomplomplomplomplomplomplomplompl	omplomplomplomplomplomplomplomplomplompl

Fig. 8D

401 394 399 399 398 391 305 262	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
T V T T T T T T T T T T T T T T T T T T	L L L L L L L L L L L L L L L L L L L
	OOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOOO
	- FEXEXXEEXE
S S S S S S S S S S S S S S S S S S S	C A P E N L L C C A P E N L L C C A P E D N L L C C A P E D N L L C C A P E N L L C C A P E N L C C C A P E N L C C C A P E N L C C C A P E N L C C C A P E N L C C C C C C C C C C C C C C C C C C
A A A A A A A A A A A A A A A A A A A	E T E E E E E E E E E E E E E E E E E E
THE	00000000000000000000000000000000000000
L L L L L L L L L L L L L L L L L L L	- H H H H H H H H H H H H H H H H H H H
S S A S I I H I D I I C C C C C C C C C C C C C C C C	G G G G G G G G G G G G G G G G G G G
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	- A A B B B B B B B B B B B B B B B B B
	L L L L L L L L L L L L L L L L L L L
112 110 G A T T T T T T T T T T T T T T T T T T	12 P P P P P P P P P P P P P P P P P P P
omp12 omp8 omp5 omp11 omp10 omp15 omp7 omp7	omp12 omp8 omp5 omp11 omp11 omp16 omp7 omp15

500 4494 4994 514 514 396 265	0 8 2 4 4 4 4 8 0 8 0 8 0 8 0 8 0 8 0 8 0 0 8 0
Q A D S R L E M D V G T T L E P - A D T S T I N N L V I N I S I D 50 Q T A G S S V I M D A G T T L E P - A D T S T I N N L V I N I S L G 49 Q V E G S K V V M D G G T T F E A S A E G V T L T G L S I P V D S L G 49 Q T E G S T L L M D A G T T L E T - A D G I T I N N L V V D L S A L E 49 Q S P G S T L L M D A G T T L E T - A D G I T I N N L V L N V D S L K 49 Q E A G S L L G M D S G T T L S T T A G S I T I T N L G I N V D S L K 49 Q E P E S T L L L D L G T S L V A N T E S I T I T N L G I N A D T I Y 51 Q D A N S K L I M D L G T K L I A S K E D I A I T G L A I D I D S L S A 8 Q E A S S T L T M S P G T T L L C S G D A - R V Q N L H I L I E 39	44444000041
OH>FOREDOE	· JOSHSSHHH · ·
G V T L D T K G V T L L D T K G G V T L L D T K G G V T L L T T Q G G V T L L T T Q G G V T L I T Q G G V T L I T Q G G V T L I T Q G G V T L I T Q G G V T L I T Q G G V T L I T Q G G V T L I T Q G G V T L G S T G G V T L G S T G G V T L G S T G G V T L G S T G G V T L G S T G G V T L G S T G G V T L G S T G G V T L G S T G G V T L G S T G G G V T L G G G V T L G G G V T L G G G V T L G G G V T L G G G V T L G G G V T L G G G V T L G G G V T L G G G V T L G G G V T G G G G G G G G G G G G G G G	A K I E T K A A B A C S L T K A A T L K A A T A C C C C C C C C C C C C C C C C
12	12
omp12 omp8 omp5 omp11 omp11 omp15 omp7 omp7 omp7	omp12 omp8 omp5 omp11 omp11 omp4 omp15 omp15

Fig. 8F

590 591 591 592 593 576 576 576	640 641 641 641 641 641 641 543 514
S T T T T T T T T T T T T T T T T T T T	I SE TE SE
H T T M M M M M M M M M M M M M M M M M	
H Y G Y Q G T W B H Y G Y Q G T W G Y Q G T W B E Y Q G Y W W A B E Y G G Y Q G W W A B E Y G G Y Q G W W A B C Y Q G K W W A	G G G G G G G G G G G G G G G G G G G
THENDER STEEL STEE	S L C V P N N L L W W W W C L V V P P N N S L L V V V V V V V V V V V V V V V V V
S T A V T P	Y Y K K K K K K K K K K K K K K K K K K
X A S G T Y S A L G T A A S G T Y S A L G T A A T A A A T A A A T A A A T A A A T A A A T A A A D D D D	THE WAT HG LAWINT G L
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35 690 691 692 693 709 593 267 514	85 734 734 735 732 752 752 752 762
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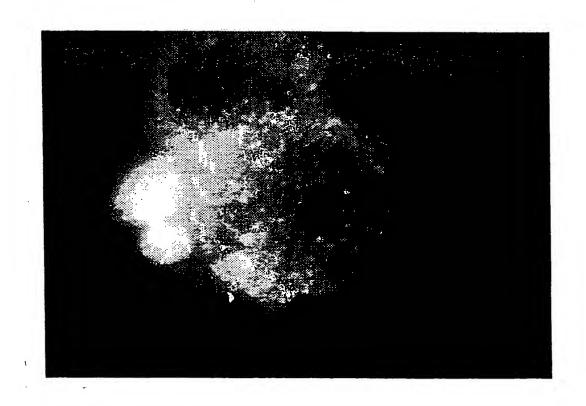
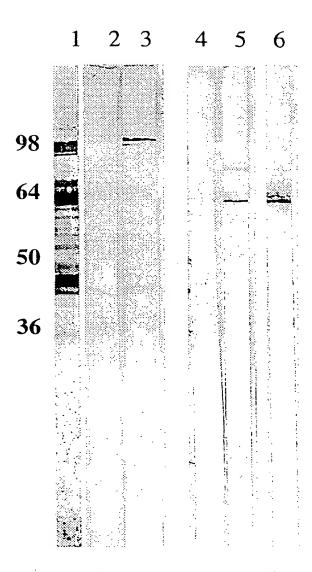


Fig. 9



Immunoblotting of *C. pneumoniae* EB, lane 1-3 heated to 100°C in SDS-sample buffer, lane 4-6 unheated. Lane 1 reacted with rabbit anti *C. pneumoniae* OMC; lane 2 and 4 pre-serum; lane 3 and 5 polyclonal rabbit anti pEX1-1 fusion protein; lane 6 MAb 26.1.

Fig. 10

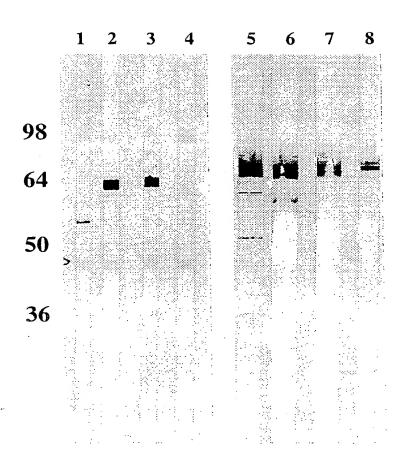


Fig. 11

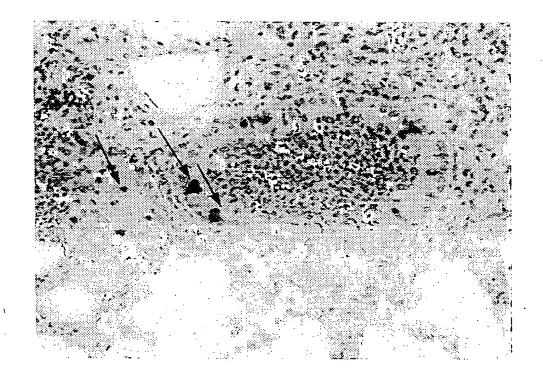


Fig. 12

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